```
=> d his

     (FILE 'HOME' ENTERED AT 12:11:19 ON 17 SEP 2004)

     FILE 'HCAPLUS' ENTERED AT 12:11:26 ON 17 SEP 2004
                E COSFORD N/AU
L1           51 E4-9
                E MCDONALD I/AU
L2          171 E3-5,E16-19
                E HESS S/AU
L3          152 E3,E5,E46-49
                E VARNEY M/AU
L4           49 E3-4,E8-10
L5        30930 (SIBIA OR MERCK)/CS,PA
L6           34 L1-4 AND EXCIT?
L7            7 L6 AND AMINO (1A) ACID?

     FILE 'REGISTRY' ENTERED AT 12:18:22 ON 17 SEP 2004

     FILE 'HCAPLUS' ENTERED AT 12:18:35 ON 17 SEP 2004
L8              TRA L7 1- RN :       351 TERMS

     FILE 'REGISTRY' ENTERED AT 12:18:36 ON 17 SEP 2004
L9           351 SEA L8
L10           99 (NCSC2 OR NSC3)/ES AND L9

     FILE 'STNGUIDE' ENTERED AT 12:21:06 ON 17 SEP 2004

=> b hcap
FILE 'HCAPLUS' ENTERED AT 12:22:22 ON 17 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
the American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 17 Sep 2004  VOL 141 ISS 13
FILE LAST UPDATED: 16 Sep 2004  (20040916/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> d all l7 tot

L7   ANSWER 1 OF 7  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2003:775879  HCAPLUS
DN   140:23399
ED   Entered STN:  03 Oct 2003
TI   Pharmacological characterization and identification of amino
     acids involved in the positive modulation of metabotropic
     glutamate receptor subtype 2
AU   Schaffhauser, Herve; Rowe, Blake A.; Morales, Sylvia; Chavez-Noriega,
     Laura E.; Yin, Ruoyuan; Jachec, Christine; Rao, Sara P.; Bain, Gretchen;
     Pinkerton, Anthony B.; Vernier, Jean-Michel; Bristow, Linda J.;
     Varney, Mark A.; Daggett, Lorrie P.
CS   Merck Research Laboratories, San Diego, CA, USA
SO   Molecular Pharmacology (2003), 64(4), 798-810
     CODEN: MOPMA3; ISSN: 0026-895X
PB   American Society for Pharmacology and Experimental Therapeutics
DT   Journal
LA   English
CC   2-2 (Mammalian Hormones)
AB   In the present study, the authors describe the characterization of a pos.
     allosteric modulator at metabotropic glutamate subtype 2 receptors
     (mGluR2).  N-4-(2-methoxyphenoxy)-phenyl-N-(2,2,2-trifluoroethylsulfonyl)-
     pyrid-3-ylmethylamine (LY 487379) is a selective pos. allosteric modulator
```

at human mGluR2 and is without activity at human mGluR3. Furthermore, LY 487379 has no intrinsic agonist or antagonist activity at hmGluR2, as determined by functional guanosine 5'(.gamma.-[35S]thio)triphosphate ([35S]GTP.gamma.S) binding, single-cell Ca2+ imaging, and electrophysiol. studies. However, LY 487379 markedly potentiated glutamate-stimulated [35S]GTP.gamma.S binding in a concentration-dependent manner at hmGluR2, shifting the glutamate dose-response curve leftward by 3-fold and increasing the maximum levels of [35S]GTP.gamma.S stimulation. This effect of LY 487479 was also observed to a greater extent on the concentration-response curves to selective hmGluR2/3 agonists. In radioligand binding studies to rat cortical membranes, LY 487379 increased the affinity of the radiolabeled agonist, [3H]DCG-IV, without affecting the binding affinity of the radio-labeled antagonist, [3H]LY341495. In rat hippocampal slices, coapplication of LY 487379 potentiated synaptically evoked mGluR2 responses. Finally, to elucidate the site of action, the authors systematically exchanged segments and single **amino acids** between hmGluR2 and hmGluR3. Substitution of Ser 688 and/or Gly 689 in transmembrane IV along with Asn 735 located in transmembrane segment V, with the homologous **amino acids** of hmGluR3, completely eliminated LY487379 allosteric modulation of hmGluR2. The authors propose that this allosteric binding site defines a pocket that is different from the orthosteric site located in the N-terminal domain.

ST metabotropic glutamate receptor 2 allosteric modulation signaling structure; glutamate mGluR2 receptor allosteric modulation signaling structure

IT Structure-activity relationship
(allosteric modulation-affecting; pharmacol. characterization and identification of **amino acids** involved in pos. modulation of metabotropic glutamate receptor subtype 2)

IT Brain
(cerebral cortex; pharmacol. characterization and identification of **amino acids** involved in pos. modulation of metabotropic glutamate receptor subtype 2)

IT Brain
(dentate gyrus; pharmacol. characterization and identification of **amino acids** involved in pos. modulation of metabotropic glutamate receptor subtype 2)

IT Neurotransmission
(glutamatergic, **excitatory**; pharmacol. characterization and identification of **amino acids** involved in pos. modulation of metabotropic glutamate receptor subtype 2)

IT Brain
(hippocampus; pharmacol. characterization and identification of **amino acids** involved in pos. modulation of metabotropic glutamate receptor subtype 2)

IT Phosphatidylinositols
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(hydrolysis; pharmacol. characterization and identification of **amino acids** involved in pos. modulation of metabotropic glutamate receptor subtype 2)

IT Glutamate receptors
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(metabotropic, group II; pharmacol. characterization and identification of **amino acids** involved in pos. modulation of metabotropic glutamate receptor subtype 2)

IT Glutamate receptors
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(metabotropic, mGluR2; pharmacol. characterization and identification of **amino acids** involved in pos. modulation of metabotropic glutamate receptor subtype 2)

IT Brain
(perforant pathway; pharmacol. characterization and identification of **amino acids** involved in pos. modulation of metabotropic glutamate receptor subtype 2)

IT Allosterism
Cell membrane
Human
Signal transduction, biological
(pharmacol. characterization and identification of **amino acids** involved in pos. modulation of metabotropic glutamate receptor subtype 2)

IT G proteins (guanine nucleotide-binding proteins)
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmacol. characterization and identification of **amino**

acids involved in pos. modulation of metabotropic glutamate receptor subtype 2)

IT Structure-activity relationship
(signal-transducing; pharmacol. characterization and identification of **amino acids** involved in pos. modulation of metabotropic glutamate receptor subtype 2)

IT Protein motifs
(transmembrane domain; pharmacol. characterization and identification of **amino acids** involved in pos. modulation of metabotropic glutamate receptor subtype 2)

IT 56-45-1, Serine, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mGluR2 receptor transmembrane IV residue 688; pharmacol. characterization and identification of **amino acids** involved in pos. modulation of metabotropic glutamate receptor subtype 2)

IT 56-40-6, Glycine, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mGluR2 receptor transmembrane IV residue 689; pharmacol. characterization and identification of **amino acids** involved in pos. modulation of metabotropic glutamate receptor subtype 2)

IT 70-47-3, Asparagine, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mGluR2 receptor transmembrane V residue 735; pharmacol. characterization and identification of **amino acids** involved in pos. modulation of metabotropic glutamate receptor subtype 2)

IT 56-86-0, Glutamic acid, biological studies 86-01-1, 5'-GTP 7440-70-2, Calcium, biological studies 15421-51-9, Inositol monophosphate 117857-93-9, LCCG-I 147782-19-2, DCG-IV 353231-17-1, LY 487379
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(pharmacol. characterization and identification of **amino acids** involved in pos. modulation of metabotropic glutamate receptor subtype 2)

RE.CNT 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Baez, M; Neuropharmacology 2002, V43, P275
(2) Birdsall, N; Biochem Soc Trans 1995, V23, P108 HCAPLUS
(3) Carlton, S; Neuroscience 2001, V105, P957 HCAPLUS
(4) Chavez-Noriega, L; Curr Drug Target CNS Neurol Disord 2002, V1, P261 HCAPLUS
(5) Chavez-Noriega, L; J Neurosci 1994, V14, P310 HCAPLUS
(6) Christopoulos, A; Pharmacol Rev 2002, V54, P323 HCAPLUS
(7) Colemna, D; US 0100643 2001
(8) Conn, P; Annu Rev Pharmacol Toxicol 1997, V37, P205 HCAPLUS
(9) Erkinjuntti, T; Lancet 2002, V359, P1283
(10) Flor, P; Eur J Neurosci 1995, V7, P622 MEDLINE
(11) Gether, U; J Biol Chem 1998, V273, P17979 HCAPLUS
(12) Gomeza, J; Mol Pharmacol 1996, V50, P923 HCAPLUS
(13) Hammerland, L; Mol Pharmacol 1998, V53, P1083 HCAPLUS
(14) Johnson, M; Neuropharmacology 2002, V43, P291
(15) Kew, J; Neuropharmacology 2001, V40, P20 HCAPLUS
(16) Kew, J; Neuropharmacology 2002, V43, P215 HCAPLUS
(17) Knoflach, F; Proc Natl Acad Sci USA 2001, V98, P13402 HCAPLUS
(18) Kowal, D; Neuropharmacology 1998, V37, P179 HCAPLUS
(19) Kunishima, N; Nature (Lond) 2000, V407, P971 HCAPLUS
(20) Lazareno, S; Br J Pharmacol 1993, V109, P1110 HCAPLUS
(21) Macek, T; J Neurophysiol 1996, V76, P3798 HCAPLUS
(22) Malherbe, P; J Biol Chem 2003, V278, P8340 HCAPLUS
(23) Monn, J; J Med Chem 1999, V42, P1027 HCAPLUS
(24) Mutel, V; J Neurochem 1998, V71, P2558 HCAPLUS
(25) Nakazato, A; J Med Chem 2000, V43, P4893 HCAPLUS
(26) Ohishi, H; J Comp Neurol 1993, V335, P252 HCAPLUS
(27) Ohishi, H; Neuroscience 1993, V53, P1009 HCAPLUS
(28) Palczewski, K; Science (Wash DC) 2000, V289, P739 HCAPLUS
(29) Pin, J; EMBO (Eur Mol Biol Organ) J 1994, V13, P342 HCAPLUS
(30) Pin, J; Eur J Pharmacol 1999, V375, P277 HCAPLUS
(31) Pin, J; Mol Pharmacol 2001, V60, P881 HCAPLUS
(32) Schaffhauser, H; Mol Pharmacol 1998, V53, P228 HCAPLUS
(33) Shepherd, T; J Med Chem 2002, V45, P2101 HCAPLUS
(34) Sigel, E; Trends Pharmacol Sci 1997, V18, P425 HCAPLUS
(35) Urwyler, S; Mol Pharmacol 2001, V60, P963 HCAPLUS
(36) Varney, M; Curr Drug Target CNS Neurol Disord 2002, V1, P283 HCAPLUS
(37) Varney, M; J Pharmacol Exp Ther 1999, V290, P170 HCAPLUS
(38) Wright, R; J Pharmacol Exp Ther 2001, V298, P453 HCAPLUS

(39) Yokoi, M; Science (Wash DC) 1996, V273, P645 HCAPLUS
(40) Ziauddin, J; Nature (Lond) 2001, V411, P107 MEDLINE

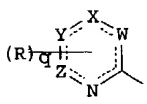
L7 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:222367 HCAPLUS
DN 138:238175
ED Entered STN: 21 Mar 2003
TI Preparation of heterocyclic compounds as metabotropic glutamate receptor 5 (mGluR5) modulators
IN **Cosford, Nicholas David Peter**; Bleicher, Leo Solomon; Vernier, Jean-Michel Andre; Cube, Rowena V.; Schweiger, Edwin J.; **McDonald, Ian**
PA Merck & Co., Inc., USA
SO U.S. Pat. Appl. Publ., 20 pp., Cont.-in-part of U.S. Ser. No. 387,073, abandoned.
CODEN: USXXCO
DT Patent
LA English
IC ICM C07D279-12
ICS C07D241-02
NCL 544059000; 544336000; 544063000; 534751000
CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 2

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003055247	A1	20030320	US 2002-217800	20020813
US 6774138	B2	20040810		
PRAI US 1999-387073	B2	19990831		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2003055247	ICM	C07D279-12
	ICS	C07D241-02
	NCL	544059000; 544336000; 544063000; 534751000
US 2003055247	ECLA	C07D213/16; C07D213/30B; C07D239/26B; C07D241/12C; C07D249/08; C07D263/32; C07D271/06B; C07D077/22C; C07D277/24; C07D277/40; C07D285/00B3; C07D333/08

OS MARPAT 138:238175
GI



I

AB The title compds. with general formula of A-L-B [wherein A = 5-7 membered ring I (where at least one of W, X, Y, and Z = (CR)p; p = 0-2; and the remainder of W, X, Y, and Z = independently O, N, S; R = halo, SH, NO2, CO2H, carbamate, carboxamide, OH, ester, CN, NH2, amide, amidine, amido, SO2, (un)substituted hydrocarbyl, aryl, or heterocyclyl); q = 0-3; L = (un)substituted alkenylene, alkynylene, or azo; B = (un)substituted (cyclo)hydrocarbyl, heterocyclyl, or aryl] and enantiomers, diastereomers, mixts., or their pharmaceutically acceptable salts thereof, which are capable of modulating the activity of **excitatory amino acid** receptors such as metabotropic glutamate receptor, are prepared Thus, reacting 2-bromo-1,3-thiazole with phenylacetylene in the presence of CuI, Et3N, and PdCl2(PPh3)2 in DME, followed by treatment of the resulting 2-(phenylethynyl)-1,3-thiazole with p-TsOH afforded 2-(phenylethynyl)-1,3-thiazole, p-TsOH salt.
ST heterocycle thiazole prepn metabotropic glutamate receptor modulator analgesic
IT **Amino acid** receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**excitatory**; preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)
IT Glutamate receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metabotropic; preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)
IT 329202-67-7P 329202-70-2P 329202-84-8P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

IT 329202-19-9P 329202-20-2P 329202-23-5P 329202-24-6P 329202-25-7P
329202-26-8P 329202-27-9P 329202-28-0P 329202-29-1P 329202-30-4P
329202-31-5P 329202-32-6P 329202-33-7P 329202-34-8P 329202-35-9P
329202-36-0P 329202-37-1P 329202-38-2P 329202-40-6P 329202-42-8P
329202-44-0P 329202-46-2P 329202-48-4P 329202-50-8P 329202-52-0P
329202-54-2P 329202-56-4P 329202-58-6P 329202-61-1P 329202-64-4P
329202-73-5P 329202-79-1P 329202-80-4P 329202-83-7P 329202-87-1P
329202-90-6P 329205-94-9P 329205-96-1P 329205-98-3P 329206-00-0P
329206-02-2P 329206-04-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

IT 78-93-3, 2-Butanone, reactions 108-50-9, 2,6-Dimethylpyrazine
115-19-5, 2-Methyl-3-butyne-2-ol 456-48-4, 3-Fluorobenzaldehyde
464-49-3 497-38-1, Norcamphor 502-42-1, Cycloheptanone 502-49-8, Cyclooctanone 536-74-3, Phenylacetylene 589-92-4, 4-Methylcyclohexanone 626-55-1, 3-Bromopyridine 627-19-0, 1-Pentyne
627-41-8, Methyl propargyl ether 917-92-0, 3,3-Dimethyl-1-butyne
931-48-6, Cyclohexylethyne 931-49-7, 1-Ethynylcyclohexene 1066-54-2, Trimethylsilylacetylene 1072-72-6, Tetrahydrothiopyran-4-one
1757-42-2, 3-Methylcyclopentanone 1945-84-2, 2-Ethynylpyridine
2320-30-1, 3,5-Dimethylcyclohexanone 2816-57-1, 2,6-Dimethylcyclohexanone 3034-48-8, 2-Bromo-5-nitro-1,3-thiazole
3034-53-5, 2-Bromo-1,3-thiazole 5315-25-3, 2-Bromo-6-methylpyridine
13223-25-1, 2-Chloro-4,6-dimethoxypyrimidine 13368-65-5 14376-79-5, 3,3,5,5-Tetramethylcyclohexanone 17356-19-3, 1-Ethynylcyclopentanol
17715-00-3, 3-Cyclohexyl-1-propyne 29943-42-8, Tetrahydro-4H-pyran-4-one
74115-12-1, 5-Chloro-3-pyridinol 111196-81-7, 2-Chloro-5-ethylpyrimidine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

IT 2510-23-8P 24202-80-0P 150145-19-0P 329202-21-3P 329202-22-4P
329202-76-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE
(1) Anon; WO 9603406 1996 HCAPLUS
(2) Anon; WO 9902497 1999
(3) Anon; WO 0116121 2001 HCAPLUS
(4) Gasparini, F; Brit. J. Pharmacology 1999, V249
(5) Shih, C; J. Med. Chem. 1992, V35, P1109 HCAPLUS
(6) Trybulski; US 4990520 A 1991 HCAPLUS
(7) Varney, M; Brit. J. Pharmacology 1999, V126(Supp), P248
(8) Varney, M; J. Med. Chem. 1997, V40, P2502 HCAPLUS
(9) Varney, M; J. Pharmacology and Exptl. Therapeutics 1999, V290, P170 HCAPLUS

L7 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:396348 HCAPLUS
DN 137:319825
ED Entered STN: 28 May 2002
TI Metabotropic glutamate receptor involvement in models of acute and persistent pain: Prospects for the development of novel analgesics
AU **Varney, M. A.**; Gereau, R. W., IV
CS Merck Research Labs - San Diego, San Diego, CA, 92121, USA
SO Current Drug Targets: CNS & Neurological Disorders (2002), 1(3), 283-296
CODEN: CDTCCC; ISSN: 1568-007X
PB Bentham Science Publishers Ltd.
DT Journal; General Review
LA English
CC 1-0 (Pharmacology)
AB A review. The **excitatory amino acid** glutamate plays a major role in nociceptive processing. Ionotropic and metabotropic glutamate receptors are expressed in relevant areas of the brain, spinal cord and periphery that are involved in pain sensation and transmission. Activation of mGlu receptors along the pain neuraxis can result in either pro-nociceptive or antinociceptive behaviors depending on the subtype of mGluR and its location. The data published to date most strongly support the idea that mGlu1 antagonists might act as

broad-spectrum analgesics. Several studies pointing to a functional upregulation of mGlu2/3 in chronic pain models suggest that agonists of these receptors might also be effective analgesics in certain conditions, most notably inflammation-induced hyperalgesia and allodynia. The expression of mGluRs throughout the pain neuraxis and the differing roles of the mGluRs in each of these regions makes it difficult to predict the efficacy of mGluR ligands based on in vitro or local administration studies. Potent, systemically active compds. that show mGluR subtype selectivity will be critical to undertake more detailed analyses in animal models of pain.

ST review metabotropic glutamate receptor analgesic drug target

IT Analgesics
Pain
(metabotropic glutamate receptor and development of analgesics)

IT Glutamate receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metabotropic; metabotropic glutamate receptor and development of analgesics)

RE.CNT 147 THERE ARE 147 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Al-Ghoul, W; Brain Res Bull 1993, V30(3-4), P453 HCAPLUS
(2) Aronica, E; Eur J Neurosci 2000, V12(7), P2333 MEDLINE
(3) Azkue, J; J Comp Neurol 2001, V430(4), P448 HCAPLUS
(4) Azkue, J; Neurosci Lett 1996, V204(1-2), P9
(5) Azkue, J; Neurosci Lett 1997, V228(1), P1 HCAPLUS
(6) Baranauskas, G; Prog Neurobiol 1998, V54(3), P349 MEDLINE
(7) Bashir, Z; Nature 1993, V363(6427), P347 HCAPLUS
(8) Baude, A; Neuron 1993, V11, P771 HCAPLUS
(9) Bennett, G; J Pain Symptom Management 2000, V19(1 Suppl), PS2 MEDLINE
(10) Bhave, G; Nat Neurosci 2001, V4(4), P417 HCAPLUS
(11) Binns, K; Neuropharmacology 2001, V40(5), P639 HCAPLUS
(12) Bleakman, D; Mol Pharmacol 1992, V42(2), P192 HCAPLUS
(13) Bordi, F; Brain Res 2000, V871(2), P223 HCAPLUS
(14) Bortolotto, Z; Nature 1994, V368(6473), P740 HCAPLUS
(15) Bortolotto, Z; Neuropharmacology 1995, V34(8), P1003 HCAPLUS
(16) Boxall, S; Neuroscience 1998, V82(2), P591 HCAPLUS
(17) Bradley, S; J Comp Neurol 1999, V407(1), P33 HCAPLUS
(18) Budai, D; Neuroscience 1998, V83(2), P571 HCAPLUS
(19) Carlton, S; Neurosci Lett 1998, V242(1), P21 HCAPLUS
(20) Carlton, S; Neuroscience 2001, V105(4), P957 HCAPLUS
(21) Cerne, R; Neurosci Lett 1992, V144(1-2), P180 HCAPLUS
(22) Cesaro, P; Eur Neurol 1997, V38(3), P209 MEDLINE
(23) Chen, J; Neurosci 2000, V98(1), P141 HCAPLUS
(24) Chen, Y; Neuroscience 2000, V95(3), P787 HCAPLUS
(25) Cherny, N; Neurology 1994, V44(5), P857 MEDLINE
(26) Chiechio, S; Mol Pharmacol 2002, V61(5), P989 HCAPLUS
(27) Chinestra, P; J Neurophysiol 1993, V70(6), P2684 HCAPLUS
(28) Coderre, T; J Neurosci 1992, V12(9), P3665 HCAPLUS
(29) Coderre, T; Neurosci Lett 1992, V140(2), P181 HCAPLUS
(30) Condorelli, D; Neurochem Res 1997, V22(9), P1127 HCAPLUS
(31) Conn, P; Ann Rev in Pharmacol Toxicol 1997, V37, P205 HCAPLUS
(32) Conquet, F; Nature 1994, V372(6503), P237 HCAPLUS
(33) Corsi, M; Metabotropic Glutamate Receptors and Brain Function 1998, P37 HCAPLUS
(34) Degroot, J; Neuroreport 2000, V11(3), P497 HCAPLUS
(35) Dogrul, A; Neurosci Lett 2000, V292(2), P115 HCAPLUS
(36) Dolan, S; Neuropharmacology 2000, V39(7), P1132 HCAPLUS
(37) Dutar, P; Neuropharmacology 1999, V38(4), P467 HCAPLUS
(38) Duvoisin, R; J Neurosci 1995, V15(4), P3075 HCAPLUS
(39) Eide, K; Pain 1995, V61(2), P221 MEDLINE
(40) Eide, P; Neurosurgery 1995, V37(6), P1080 MEDLINE
(41) Ferraguti, F; Eur J Neurosci 1999, V11, P2073 MEDLINE
(42) Fisher, K; J Pain Symptom Management 2000, V20(5), P358 MEDLINE
(43) Fisher, K; Neuroreport 1998, V9(6), P1169 HCAPLUS
(44) Fisher, K; Pain 1996, V68(2-3), P255 MEDLINE
(45) Fisher, K; Pain 1998, V77(1), P59 HCAPLUS
(46) Fotuhi, M; J Neurosci 1993, V13(5), P2001 HCAPLUS
(47) Francesconi, A; J Biol Chem 1998, V273(10), P5615 HCAPLUS
(48) Fundytus, M; Br J Pharmacol 1994, V113(4), P1215 HCAPLUS
(49) Fundytus, M; Br J Pharmacol 1997, V120(6), P1015 HCAPLUS
(50) Fundytus, M; Br J Pharmacol 2001, V132(1), P354 HCAPLUS
(51) Fundytus, M; Neuroreport 1998, V9(4), P731 HCAPLUS
(52) Gerber, G; Neuroscience 2000, V100(2), P393 HCAPLUS
(53) Hansson, P; Pain Clinical Updates 1994, VII(3, December)
(54) Harris, J; J Physiol Paris 1996, V90(1), P15 MEDLINE
(55) Hewitt, D; Clin J Pain 2000, V16(2 Suppl), PS73 MEDLINE

(56) Hofmann, H; Eur J Pharmacol 2001, V429(1-3), P135 HCAPLUS
(57) Huber, K; J Neurophysiol 2001, V86(1), P321 HCAPLUS
(58) Huber, K; Science 2000, V288(5469), P1254 HCAPLUS
(59) Hunskaar, S; J Neurosci Methods 1985, V14(1), P69 HCAPLUS
(60) Jevtovic-Todorovic, V; Nat Med 1998, V4(4), P460 HCAPLUS
(61) Jia, H; J Comp Neurol 1999, V410(4), P627 HCAPLUS
(62) Joly, C; J Neurosci 1995, V15(5 Pt 2), P3970 MEDLINE
(63) Karim, F; J Neurosci 2001, V21(11), P3771 HCAPLUS
(64) Karim, F; Mol Psychiatry 2001, V6(6), P615 MEDLINE
(65) Katsurabayashi, S; J Neurophysiol 2001, V85(1), P332 HCAPLUS
(66) Kim, K; Exp Brain Res 1997, V113(2), P200 MEDLINE
(67) Knoflach, F; J Physiol 1998, V509(Pt 2), P347
(68) Kristensen, P; Neurosci Lett 1993, V155(2), P159 HCAPLUS
(69) Lawand, N; Pain 2000, V86(1-2), P69 HCAPLUS
(70) Li, H; Neurosci Lett 1997, V223(3), P153 HCAPLUS
(71) Li, J; Neurosci Lett 1996, V204(1-2), P9 MEDLINE
(72) Macdonald, N; Recent Results Cancer Res 1991, V121, P24 MEDLINE
(73) Maione, S; Pain 2000, V85(1-2), P183 HCAPLUS
(74) Malmberg, A; Science 1997, V278, P279 HCAPLUS
(75) Mao, J; Brain Res 1992, V588(1), P144 HCAPLUS
(76) Martin, L; Neuron 1992, V9(2), P259 HCAPLUS
(77) Martin, W; J Neurosci 2001, V21(14), P5321 HCAPLUS
(78) Martin, W; Neuroscience 1999, V88(4), P1267 HCAPLUS
(79) McQuay, H; Acta Anaesthesiol Scand 1997, V41(1 Pt 2), P175 MEDLINE
(80) McQuay, H; Anaesthesia 1992, V47(9), P757 MEDLINE
(81) Mills, C; Exp Neurol 2001, V170(2), P244 HCAPLUS
(82) Mills, C; Exp Neurol 2002, V173(1), P153 HCAPLUS
(83) Mills, C; Neuroreport 2000, V11(14), P3067 HCAPLUS
(84) Morisset, V; J Neurophysiol 1996, V76(4), P2794 HCAPLUS
(85) Nakajima, Y; J Biol Chem 1993, V268(16), P11868 HCAPLUS
(86) Neto, F; Neurosci Lett 2000, V296(1), P25 HCAPLUS
(87) Neugebauer, V; Eur J Neurosci 1994, V6(7), P1179 MEDLINE
(88) Neugebauer, V; J Neurophysiol 1996, V76(6), P3740 HCAPLUS
(89) Neugebauer, V; J Neurophysiol 1999, V82(1), P272 HCAPLUS
(90) Neugebauer, V; J Neurophysiol 2000, V84(6), P2998 HCAPLUS
(91) Nikolajsen, L; Anesth Analg 2000, V91(4), P960 HCAPLUS
(92) Nikolajsen, L; Pain 1996, V67(1), P69 HCAPLUS
(93) Ohishi, H; Neurosci Lett 1995, V202(1-2), P85 MEDLINE
(94) Oliet, S; Neuron 1997, V18(6), P969 HCAPLUS
(95) Ossipov, M; Neurosci Lett 1995, V199(2), P83 HCAPLUS
(96) Ossipov, M; Pain 1995, V62(3), P287 HCAPLUS
(97) O'Leary, D; Neurosci Lett 1997, V229(1), P29 HCAPLUS
(98) Palazzo, E; Neuropharmacology 2001, V40(3), P319 HCAPLUS
(99) Pan, Z; Nature 1997, V389(6649), P382 HCAPLUS
(100) Peavy, R; J Neurochem 1998, V71, P603 HCAPLUS
(101) Petralia, R; J Chem Neuroanat 1997, V13(2), P77 HCAPLUS
(102) Petralia, R; Neuroscience 1996, V71(4), P949 HCAPLUS
(103) Popik, P; Br J Pharmacol 2000, V130(6), P1425 HCAPLUS
(104) Portenoy, R; Lancet 1992, V339(8800), P1026 MEDLINE
(105) Ren, K; J Orofac Pain 1999, V13(3), P155 MEDLINE
(106) Romano, C; J Comp Neurol 1995, V355(3), P455 HCAPLUS
(107) Russo, R; J Physiol 1997, V499(Pt 2), P459
(108) Russo, R; Neuroscience 1994, V61(2), P191 HCAPLUS
(109) Salt, T; Exp Brain Res 1998, V121(2), P181 HCAPLUS
(110) Salt, T; Neuropharmacology 1995, V34(8), P1043 HCAPLUS
(111) Salt, T; Neuropharmacology 1996, V35(2), P239 HCAPLUS
(112) Salt, T; Neuroscience 1995, V65(1), P5 HCAPLUS
(113) Salt, T; Neuroscience 1998, V85(3), P655 HCAPLUS
(114) Salt, T; Neuroscience 2000, V100(2), P375 HCAPLUS
(115) Saugstad, J; J Neurosci 1996, V16(19), P5979 HCAPLUS
(116) Scarpini, E; J Peripher Nerv Syst 1997, V2(3), P250 HCAPLUS
(117) Seltzer, Z; Pain 1990, V43(2), P205 MEDLINE
(118) Shigemoto, R; Neurosci Lett 1993, V163(1), P53 HCAPLUS
(119) Sillevis, S; New Eng J Med 2000, V342(1), P21
(120) Silva, G; Neurosci Lett 1999, V263(2-3), P117 MEDLINE
(121) Sladeczek, F; Nature 1985, V317(6039), P717 HCAPLUS
(122) Stanfa, L; Eur J Pharmacol 1998, V347(2-3), P165 MEDLINE
(123) Tamaru, Y; Neuroscience 2001, V106(3), P481 HCAPLUS
(124) Tang, F; Neurosci Res 1999, V34(2), P73 HCAPLUS
(125) Thomas, N; Neuropharmacology 2001, V40(3), P311 HCAPLUS
(126) Tjolsen, A; Pain 1992, V51(1), P5 MEDLINE
(127) Tomiyama, M; J Neurol Sci 2001, V189(1-2), P65 HCAPLUS
(128) Trujillo, K; Science 1991, V251(4989), P85 HCAPLUS
(129) Vaccarino, A; Brain Res 1994, V666(1), P104 HCAPLUS
(130) Valerio, A; Neuroreport 1997, V8(12), P2695 HCAPLUS
(131) Valerio, A; Neuroscience Res 1997, V28(1), P49 MEDLINE

(132) Vandergriff, J; Neuropharmacology 1999, V38(2), P217 HCAPLUS
(133) Varney, M; J Pharmacol Exp Ther 1999, V290(1), P170 HCAPLUS
(134) Vidnyanszky, Z; Neuroreport 1994, V6(1), P209 HCAPLUS
(135) Walker, K; Neuropharmacology 2001, V40(1), P1 HCAPLUS
(136) Walker, K; Neuropharmacology 2001, V40(1), P10 HCAPLUS
(137) Watkins, L; Trends Neurosci 2001, V24(8), P450 HCAPLUS
(138) Yashpal, K; J Neurosci 1995, V15(5 Pt 1), P3263 MEDLINE
(139) Yashpal, K; Pain 2001, V94(1), P17 HCAPLUS
(140) Yezierski, R; Pain 1996, V68(2-3), P185 MEDLINE
(141) Yi, P; Neurosci Lett 1995, V185(3), P207 HCAPLUS
(142) Young, M; Brain Research 1997, V777(1-2), P161 MEDLINE
(143) Young, M; J Neurosci 1998, V18(23), P10180 HCAPLUS
(144) Young, M; Neuropharmacology 1995, V34(8), P1033 HCAPLUS
(145) Zhang, L; J Pharmacol Exp Ther 2002, V300(1), P149 HCAPLUS
(146) Zhong, J; Brain Res 2000, V887(2), P359 HCAPLUS
(147) Zhou, S; Brain Res 2001, V913(1), P18 HCAPLUS

L7 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:167983 HCAPLUS
DN 134:222706
ED Entered STN: 09 Mar 2001
TI Preparation of heterocyclic compounds as metabotropic glutamate receptor 5 (mGluR5) modulators
IN **Cosford, Nicholas D. P.**; **McDonald, Ian A.**; Bleicher, Leo Solomon; Cube, Rowena V.; Schweiger, Edwin J.; Vernier, Jean-Michel; **Hess, Stephen D.**; **Varney, Mark A.**; Munoz, Benito
PA Merck & Co., Inc., USA
SO PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D277-22
ICS C07D277-24; C07D277-40; C07D213-16; C07D213-30; C07D239-26; C07D263-32; C07D271-06; C07D241-12; C07D249-08; C07D285-00; C07D333-08; C07D417-06; C07D409-06; C07D407-06
CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

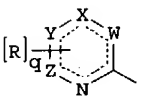
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001016121	A1	20010308	WO 2000-US23923	20000831
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1214303	A1	20020619	EP 2000-957932	20000831
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003508390	T2	20030304	JP 2001-519688	20000831
PRAI	US 1999-387073	A2	19990831		
	US 1999-387135	A2	19990831		
	WO 2000-US23923	W	20000831		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001016121	ICM	C07D277-22
	ICS	C07D277-24; C07D277-40; C07D213-16; C07D213-30; C07D239-26; C07D263-32; C07D271-06; C07D241-12; C07D249-08; C07D285-00; C07D333-08; C07D417-06; C07D409-06; C07D407-06

OS MARPAT 134:222706
GI



I.

AB The title compds. I [ALB; A = 5-7 membered ring II (wherein at least one of W, X, Y and Z = (CR)p; p = 0-2, and the remainder of W, X, Y and Z = O, N, S; R = halo, (un)substituted aryl, heterocyclyl, etc.); L = (un)substituted alkenylene, alkynylene, azo; B = (un)substituted alkyl, cycloalkyl, heterocyclyl, etc.] and their pharmaceutically acceptable salts which are capable of modulating the activity of **excitatory amino acid** receptors such as metabotropic glutamate receptor, were prepared Thus, reacting 2-bromo-1,3-thiazole with phenylacetylene in the presence of CuI, Et3N and PdCl2(PPh3)2 in DME followed by treatment of the resulting 2-(phenylethynyl)-1,3-thiazole with p-TsOH afforded 2-(phenylethynyl)-1,3-thiazole, p-TsOH salt which showed IC50 of 0.1 nM - 10 .mu.M in Ca+2 flux assay and analgesic efficacy in analgesic animal model (CFA model).

ST heterocycle prepn metabotropic glutamate receptor modulator analgesic

IT Glutamate receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(metabotropic, mGluR5; preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

IT Analgesics
(preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

IT 329202-67-7P 329202-70-2P 329202-84-8P 329203-16-9P 329203-45-4P
329203-62-5P 329204-13-9P 329204-29-7P 329204-39-9P 329204-47-9P
329204-85-5P 329204-87-7P 329204-97-9P 329205-38-1P 329205-42-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

IT 24622-44-4P 35070-01-0P 111600-92-1P 129610-15-7P 329202-19-9P
329202-20-2P 329202-23-5P 329202-24-6P 329202-25-7P 329202-26-8P
329202-27-9P 329202-28-0P 329202-29-1P 329202-30-4P 329202-31-5P
329202-32-6P 329202-33-7P 329202-34-8P 329202-35-9P 329202-36-0P
329202-37-1P 329202-38-2P 329202-40-6P 329202-42-8P 329202-44-0P
329202-46-2P 329202-48-4P 329202-50-8P 329202-52-0P 329202-54-2P
329202-56-4P 329202-58-6P 329202-61-1P 329202-64-4P 329202-73-5P
329202-79-1P 329202-80-4P 329202-83-7P 329202-87-1P 329202-90-6P
329202-93-9P 329202-98-4P 329203-01-2P 329203-02-3P 329203-05-6P
329203-06-7P 329203-10-3P 329203-13-6P 329203-19-2P 329203-22-7P
329203-25-0P 329203-28-3P 329203-31-8P 329203-36-3P 329203-39-6P
329203-42-1P 329203-48-7P 329203-51-2P 329203-54-5P 329203-57-8P
329203-59-0P 329203-65-8P 329203-78-3P 329203-80-7P 329203-91-0P
329203-94-3P 329203-98-7P 329204-01-5P 329204-02-6P 329204-07-1P
329204-10-6P 329204-16-2P 329204-19-5P 329204-22-0P 329204-25-3P
329204-27-5P 329204-31-1P 329204-33-3P 329204-36-6P 329204-41-3P
329204-43-5P 329204-45-7P 329204-49-1P 329204-51-5P 329204-53-7P
329204-55-9P 329204-57-1P 329204-59-3P 329204-62-8P 329204-64-0P
329204-66-2P 329204-72-0P 329204-75-3P 329204-82-2P 329204-89-9P
329204-91-3P 329204-95-7P 329204-99-1P 329205-01-8P 329205-03-0P
329205-05-2P 329205-07-4P 329205-09-6P 329205-11-0P 329205-13-2P
329205-15-4P 329205-17-6P 329205-19-8P 329205-21-2P 329205-23-4P
329205-28-9P 329205-31-4P 329205-34-7P 329205-40-5P 329205-44-9P
329205-46-1P 329205-48-3P 329205-50-7P 329205-52-9P 329205-54-1P
329205-56-3P 329205-58-5P 329205-60-9P 329205-62-1P 329205-64-3P
329205-66-5P 329205-68-7P 329205-71-2P 329205-74-5P 329205-77-8P
329205-84-7P 329205-86-9P 329205-88-1P 329205-90-5P 329205-92-7P
329205-94-9P 329205-96-1P 329205-98-3P 329206-00-0P 329206-02-2P
329206-04-4P 329206-11-3P 329206-13-5P 329206-16-8P 329206-18-0P
329206-20-4P 329206-22-6P 329206-24-8P 329214-37-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

IT 70-23-5, Ethyl bromopyruvate 78-93-3, 2-Butanone, reactions 78-95-5, Chloroacetone 83-33-0, 1-Indanone 92-66-0, 4-Bromobiphenyl 98-80-6, Phenylboronic acid 100-58-3, Phenylmagnesium bromide 107-19-7, Propargyl alcohol 108-50-9, 2,6-Dimethylpyrazine 108-79-2, 4,6-Dimethyl-2-hydroxypyrimidine 109-01-3, 1-Methylpiperazine 110-89-4, Piperidine, reactions 115-19-5, 2-Methyl-3-butyne-2-ol 118-92-3, Anthranilic acid 120-72-9, Indole, reactions 126-81-8, 5,5-Dimethyl-1,3-cyclohexanedione 141-30-0, 3,6-Dichloropyridazine 352-13-6, 4-Fluorophenylmagnesium bromide 456-48-4, 3-Fluorobenzaldehyde 464-49-3 497-38-1, Norcamphor 502-42-1, Cycloheptanone 502-49-8,

Cyclooctanone 529-34-0, .alpha.-Tetralone 530-93-8, .beta.-Tetralone 536-74-3, Phenylacetylene 585-36-4, 3-Trifluoromethylcyclohexanone 589-92-4, 4-Methylcyclohexanone 615-13-4, 2-Indanone 621-79-4, Cinnamamide 622-31-1, syn-Benzaldehyde oxime 623-49-4, Ethyl cyanoformate 624-28-2, 2,5-Dibromopyridine 625-92-3, 3,5-Dibromopyridine 626-55-1, 3-Bromopyridine 627-19-0, 1-Pentyne 627-41-8, Methyl propargyl ether 693-95-8, 4-Methylthiazole 766-49-4, Benzene, 1-ethynyl-2-fluoro- 766-82-5, Benzene, 1-ethynyl-3-methyl 766-98-3, 1-Ethynyl-4-fluorobenzene 917-92-0, 3,3-Dimethyl-1-butyne 931-48-6, Cyclohexylethyne 931-49-7, 1-Ethynylcyclohexene 1066-54-2, Trimethylsilylacetylene 1072-72-6, Tetrahydrothiopyran-4-one 1080-32-6, Diethylbenzyl phosphonate 1193-18-6, 3-Methyl-2-cyclohexen-1-one 1532-97-4, 4-Bromoisoquinoline 1679-18-1, 4-Chlorophenylboronic acid 1692-15-5, Pyridine-4-boronic acid 1692-25-7, Pyridine-3-boronic acid 1757-42-2, 3-Methylcyclopentanone 1945-84-2, 2-Ethynylpyridine 2320-30-1, 3,5-Dimethylcyclohexanone 2816-57-1, 2,6-Dimethylcyclohexanone 3034-48-8, 2-Bromo-5-nitro-1,3-thiazole 3034-53-5, 2-Bromo-1,3-thiazole 3581-91-7, 4,5-Dimethyl-1,3-thiazole 4175-77-3, 2,4-Dibromo-1,3-thiazole 4341-24-6, 5-Methyl-1,3-cyclohexanedione 4360-47-8, Cinnamonitrile 4526-06-1 4595-59-9, 5-Bromopyrimidine 4595-60-2, 2-Bromopyrimidine 4637-24-5 4832-17-1, 2-Decalone 5315-25-3, 2-Bromo-6-methylpyridine 5323-87-5, 3-Ethoxy-2-cyclohexen-1-one 5720-07-0, 4-Methoxyphenylboronic acid 5927-18-4, Trimethylphosphonoacetate 6622-92-0, 2,4-Dimethyl-6-hydroxypyrimidine 6651-36-1 6672-30-6 7214-52-0, cis-3,5-Dimethylcyclohexanone 10472-24-9, Methyl 2-oxocyclopentanecarboxylate 13139-86-1, 4-Anisylmagnesium bromide 13223-25-1, 2-Chloro-4,6-dimethoxypyrimidine 13368-65-5 13472-85-0, 5-Bromo-2-methoxypyridine 13575-75-2, 6,7-Dimethoxy-1-tetralone 14376-79-5, 3,3,5,5-Tetramethylcyclohexanone 14630-40-1, Bis(trimethylsilyl)acetylene 16114-47-9, 3,5-Dimethyl-4-isoxazolylboronic acid 16494-36-3, 2-Iodo-5-methylthiophene 16982-21-1, Ethyl thiooxamate 17356-19-3, 1-Ethynylcyclopentanol 17715-00-3, 3-Cyclohexyl-1-propyne 18871-66-4, N,N-Dimethylacetamide dimethylacetal 19550-72-2, cis-3,4-Dimethylcyclopentanone 20826-04-4, 5-Bromonicotinic acid 23380-78-1 29943-42-8, Tetrahydro-4H-pyran-4-one 32111-21-0, 2-Iodopyrazine 32499-64-2 34259-99-9, 4-Bromo-1,3-thiazole 35590-37-5, 5-Bromonicotinonitrile 38945-21-0, O-Allylhydroxylamine hydrochloride 52482-10-7 54390-97-5, 5-Bromoisothiazole 58372-16-0 69045-79-0, 2-Chloro-5-iodopyridine 74115-12-1, 5-Chloro-3-pyridinol 81166-84-9, Cyclopropyl trimethylsilylacetylene 89878-14-8, Diethyl(3-pyridyl)borane 109299-78-7, (5-Pyrimidinyl)boronic acid 111196-81-7, 2-Chloro-5-ethylpyrimidine 223425-52-3 329206-68-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

IT 694-82-6P 698-16-8P 2510-23-8P 6267-39-6P 6436-59-5P 7210-73-3P 7214-50-8P 13750-63-5P 13750-68-0P 18245-82-4P 20949-84-2P 24202-80-0P 27012-25-5P 29681-44-5P 29947-24-8P 35023-83-7P 40019-47-4P 65832-21-5P 68790-38-5P 74965-38-1P 76632-23-0P 86521-14-4P 86521-15-5P 111600-83-0P 117637-81-7P 123994-49-0P 127053-31-0P 150145-19-0P 154499-80-6P 170859-78-6P 176648-09-2P 179076-90-5P 183608-47-1P 184368-73-8P 193631-86-6P 228405-66-1P 256637-49-7P 291763-66-1P 329202-21-3P 329202-22-4P 329202-76-8P 329203-70-5P 329203-75-0P 329203-85-2P 329203-88-5P 329204-05-9P 329204-69-5P 329204-78-6P 329204-80-0P 329204-93-5P 329205-26-7P 329205-36-9P 329205-79-0P 329205-81-4P 329206-36-2P 329206-38-4P 329206-40-8P 329206-42-0P 329206-45-3P 329206-48-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Agouron Pharma; WO 9603406 A 1996 HCAPLUS
(2) Gasparini; BRITISH JOURNAL OF PHARMACOLOGY 1999, V126(SUPPL PROC), P249
(3) Novartis Erfindungen Verwaltun; WO 9902497 A 1999
(4) Shih; HCAPLUS
(5) Shih; J MED CHEM 1992, V35(6), P1109 HCAPLUS
(6) Varney; HCAPLUS
(7) Varney; BRITISH JOURNAL OF PHARMACOLOGY 1999, V126(SUPPL PROC), P248
(8) Varney; J MED CHEM 1997, V40(16), P2502 HCAPLUS
(9) Varney, M; JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS 1999, V290(1), P170 HCAPLUS

L7 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:335459 HCAPLUS
DN 131:125342
ED Entered STN: 02 Jun 1999
TI (R,S)-4-phosphonophenylglycine, a potent and selective group III metabotropic glutamate receptor agonist, is anticonvulsive and neuroprotective in vivo
AU Gasparini, F.; Bruno, V.; Battaglia, G.; Lukic, S.; Leonhardt, T.; Inderbitzin, W.; Laurie, D.; Sommer, B.; **Varney, M. A.**; **Hess, S. D.**; Johnson, E. C.; Kuhn, R.; Urwyler, S.; Sauer, D.; Portet, C.; Schmutz, M.; Nicoletti, F.; Flor, P. J.
CS Nervous System Research, Novartis Pharma AG, Basel, Switz.
SO Journal of Pharmacology and Experimental Therapeutics (1999), 289(3), 1678-1687
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
CC 1-11 (Pharmacology)
Section cross-reference(s): 34
AB Group III metabotropic glutamate receptors (mGluRs) are thought to modulate neurotoxicity of **excitatory amino acids**, via mechanisms of presynaptic inhibition, such as regulation of neurotransmitter release. Here, we describe (R,S)-4-phosphonophenylglycine (PPG) as a novel, potent, and selective agonist for group III mGluRs. In recombinant cell lines expressing the human receptors hmGluR4a, hmGluR6, hmGluR7b, or hmGluR8a, EC50 values for (R,S)-PPG of 5.2.+-.0.7 .mu.M, 4.7.+-.0.9 .mu.M, 185.+-.42 .mu.M, and 0.2.+-.0.1 .mu.M, resp., were measured. The compound showed EC50 and IC50 values of .gtoreq.200 .mu.M at group I and II hmGluRs and was inactive at cloned human N-methyl-D-aspartate, .alpha.-amino-3-hydroxy-5-methyl-isoxazole-4-propionate, and kainate receptors (>300 .mu.M). On the other hand, it showed micromolar affinity for a Ca2+/Cl--dependent L-glutamate binding site in rat brain, similar to other phosphono-substituted **amino acids** like L-2-amino-4-phosphonobutyrate. In cultured cortical neurons, (R,S)-PPG provided protection against a toxic pulse of N-methyl-D-aspartate (EC50 = 12 .mu.M), which was reversed by the group III mGluR antagonist (R,S)-.alpha.-methylserine-O-phosphate but not by the group II antagonist (2S)-.alpha.-ethylglutamate. Moreover, (R,S)-PPG protected against N-methyl-D-aspartate- and quinolinic acid-induced striatal lesions in rats and was anticonvulsive in the maximal electroshock model in mice. In contrast to the group III mGluR agonists L-2-amino-4-phosphonobutyrate and L-serine-O-phosphate, (R,S)-PPG showed no proconvulsive effects (2200 nmol i.c.v.). These data provide novel in vivo evidence for group III mGluRs as attractive targets for neuroprotective and anticonvulsive therapy. Also, (R,S)-PPG represents an attractive tool to analyze the roles of group III mGluRs in nervous system physiol. and pathol.
ST phosphonophenylglycine metabotropic glutamate receptor agonist anticonvulsive neuroprotective
IT Anticonvulsants
((R,S)-4-phosphonophenylglycine anticonvulsive and neuroprotective activity, and relation to group III metabotropic glutamate receptors)
IT Glutamate receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(metabotropic, inhibitors; (R,S)-4-phosphonophenylglycine anticonvulsive and neuroprotective activity, and relation to group III metabotropic glutamate receptors)
IT Cytoprotective agents
(neuroprotectants; (R,S)-4-phosphonophenylglycine anticonvulsive and neuroprotective activity, and relation to group III metabotropic glutamate receptors)
IT Toxicity
(neurotoxicity; (R,S)-4-phosphonophenylglycine anticonvulsive and neuroprotective activity, and relation to group III metabotropic glutamate receptors)
IT 120667-15-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
((R,S)-4-phosphonophenylglycine anticonvulsive and neuroprotective activity, and relation to group III metabotropic glutamate receptors)
IT 123-08-0, 4-Hydroxybenzaldehyde
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; (R,S)-4-phosphonophenylglycine anticonvulsive and neuroprotective activity, and relation to group III metabotropic

glutamate receptors)
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Abdul-Ghani, A; Brain Res 1997, V755, P202 HCAPLUS
(2) Bedingfield, J; Eur J Pharmacol 1996, V309, P71 HCAPLUS
(3) Bigge, C; J Med Chem 1989, V32, P1580 HCAPLUS
(4) Bruno, V; Eur J Pharmacol 1996, V310, P61 HCAPLUS
(5) Colwell, C; Brain Res 1996, V726, P223 HCAPLUS
(6) Conn, P; Annu Rev Pharmacol Toxicol 1997, V37, P205 HCAPLUS
(7) Copani, A; Mol Pharmacol 1995, V47, P890 HCAPLUS
(8) Daggett, L; Soc Neurosci Abst 1996
(9) Difiglia, M; Trends Neurol Sci 1990, V13, P286 MEDLINE
(10) Duvoisin, R; J Neurosci 1995, V15, P3075 HCAPLUS
(11) Faden, A; J Neurotrauma 1997, V14, P885 MEDLINE
(12) Fagg, G; J Neurosci 1982, V2, P958 HCAPLUS
(13) Flor, P; J Neurochem 1996, V67, P58 HCAPLUS
(14) Flor, P; Neuropharmacology 1997, V36, P153 HCAPLUS
(15) Ghauri, M; Neuroreport 1996, V7, P1469 HCAPLUS
(16) Graham, M; Eur J Pharmacol 1994, V288, P115 HCAPLUS
(17) Hollmann, M; Annu Rev Neurosci 1994, V17, P31 HCAPLUS
(18) Jane, D; Neuropharmacology 1996, V35, P1029 HCAPLUS
(19) Johansen, P; Mol Pharmacol 1995, V48, P140 HCAPLUS
(20) Knopfel, T; Eur J Pharmacol 1995, V288, P389 MEDLINE
(21) Kupferberg, H; Epilepsy:A Comprehensive Textbook 1997, V2, P1417
(22) Laurie, D; Naunyn Schmiedeberg's Arch Pharmacol 1995, V351, P565 HCAPLUS
(23) Laurie, D; Neuropharmacology 1997, V36, P145 HCAPLUS
(24) Lin, F; Neuropharmacology 1997, V36, P917 HCAPLUS
(25) Lipton, S; N Engl J Med 1994, V330, P613 HCAPLUS
(26) Martin, G; J Neurophysiol 1997, V78, P3028 HCAPLUS
(27) Monn, J; J Med Chem 1997, V40, P528 HCAPLUS
(28) Monyer, H; Neuron 1992, V8, P967 HCAPLUS
(29) Okamoto, N; J Biol Chem 1994, V269, P1231 HCAPLUS
(30) Sauer, D; J Neurosci Methods 1992, V42, P69 HCAPLUS
(31) Shigemoto, R; J Neurosci 1997, V17, P7503 HCAPLUS
(32) Tanabe, Y; Neuron 1992, V8, P169 HCAPLUS
(33) Tang, E; Eur J Pharmacol 1997, V327, P109 HCAPLUS
(34) Thomas, N; Neuropharmacology 1996, V35, P637 HCAPLUS
(35) Trombley, P; J Neurosci 1992, V12, P2043 HCAPLUS
(36) Urwyler, S; Neuropharmacology 1996, V35, P643 HCAPLUS
(37) Urwyler, S; Neuropharmacology 1996, V35, P655 HCAPLUS
(38) Varney, M; J Pharmacol Exp Ther 1996, V279, P367 HCAPLUS
(39) Varney, M; J Pharmacol Exp Ther 1998, V285, P358 HCAPLUS
(40) Watkins, J; Trends Pharmacol Sci 1990, V11, P25 HCAPLUS
(41) Wu, S; Mol Brain Res 1998, V53, P88 HCAPLUS

L7 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1993:531539 HCAPLUS
DN 119:131539
ED Entered STN: 02 Oct 1993
TI Potentiation of NMDA antagonists with probenecid
IN **McDonald, Ian A.**; Baron, Bruce M.
PA Merrell Dow Pharmaceuticals, Inc., USA
SO PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-19
ICS A61K031-405; A61K031-445; A61K031-66
CC 1-11 (Pharmacology)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9312780	A1	19930708	WO 1992-US10354	19921201
	W: AU, CA, JP, KR, NZ				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	US 5318985	A	19940607	US 1991-811204	19911220
	AU 9331509	A1	19930728	AU 1993-31509	19921201
	AU 667333	B2	19960321		
	EP 617616	A1	19941005	EP 1992-925469	19921201
	EP 617616	B1	19991027		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 07504890	T2	19950601	JP 1992-511664	19921201
	AT 185969	E	19991115	AT 1992-925469	19921201
	US 5489579	A	19960206	US 1994-191996	19940204
PRAI	US 1991-811204		19911220		
	WO 1992-US10354		19921201		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9312780	ICM	A61K031-19
	ICS	A61K031-405; A61K031-445; A61K031-66

OS MARPAT 119:131539

AB Probenecid potentiates the therapeutic activity of known antagonists of NMDA receptor-**excitatory amino acids.** The antagonists comprise 4 classes of compds. (Markush structures given), such as carboxyindoles, phosphonates and carboxypiperidines. The compns. comprising probenecid and the antagonists are useful for the treatment of epilepsy, neurodegenerative diseases, anxiety, etc. Probenecid potentiated the ability of (R)-4-oxo-5-phosphononorvaline to inhibit quinolinic acid-induced clonic seizures in mice.

ST NMDA antagonist probenecid antiepileptic; neurodegenerative disease drug NMDA antagonist probenecid

IT Neurotransmitter antagonists
(**excitatory amino acid**/NMDA, probenecid potentiation of)

IT Nervous system agents
(for treatment of neurodegenerative diseases, compns. containing probenecid with antagonist of NMDA receptor-**excitatory amino acids**)

IT Analgesics
Anticonvulsants and Antiepileptics
Anxiolytics
(probenecid mixts. with antagonist of NMDA receptor-**excitatory amino acids**)

IT Brain, disease
(ischemia, treatment of, with compns. containing probenecid and antagonist of NMDA receptor-**excitatory amino acids**)

IT 149890-43-7 149890-44-8
RL: BIOL (Biological study)
(antiepileptic)

IT 57-66-9D, Probenecid, mixture with antagonists of NMDA receptor-**excitatory amino acids**
RL: BIOL (Biological study)
(epilepsy and neurodegenerative diseases treatment by)

L7 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1991:17877 HCAPLUS

DN 114:17877

ED Entered STN: 26 Jan 1991

TI Activity of 5,7-dichlorokynurenic acid, a potent antagonist at the N-methyl-D-aspartate receptor-associated glycine binding site

AU Baron, Bruce M.; Harrison, Boyd L.; Miller, Francis P.; **McDonald, Ian A.**; Salituro, Francesco G.; Schmidt, Christopher J.; Sorensen, Stephen M.; White, H. Steven; Palfreyman, Michael G.

CS Merrell Dow Res. Inst., Cincinnati, OH, 45215, USA

SO Molecular Pharmacology (1990), 38(4), 554-61
CODEN: MOPMA3; ISSN: 0026-895X

DT Journal

LA English

CC 2-8 (Mammalian Hormones)
Section cross-reference(s): 1

AB 5,7-Dichlorokynurenic acid (5,7-DCKA), one of the most potent **excitatory amino acid** receptor antagonists yet described, binds to a strychnine-insensitive glycine binding site located on the N-methyl-D-aspartate (NMDA) receptor complex (Ki = 79 nM vs. [3H]glycine). 5,7-DCKA (10 .mu.M) antagonized the ability of NMDA to stimulate the binding of the radiolabeled ion channel blocker N-[3H]-[1-(2-thienyl)cyclohexyl]-piperidine ([3]TCP). Glycine overcame this effect and in the presence of 5,7-DCKA enhanced [3H]TCP binding to antagonist-free levels. 5,7-DCKA completely and noncompetitively antagonized several NMDA receptor-mediated biochem. and electrophysiol. responses. Thus, micromolar concns., 5,7-DCKA inhibited: NMDA-stimulated elevation of cytosolic Ca in cultured hippocampal neurons, cGMP accumulation in cerebellar slices, and norepinephrine release from hippocampal slices. The glycine antagonist could also block the action of synaptically released agonist, as shown by its ability to inhibit the increase in the magnitude of the population spike that follows tetanic stimulation of the hippocampus in vitro (long term potentiation). Inclusion of glycine or D-serine prevented all these effects of the antagonist. 5,7-DCKA was a potent anticonvulsant when administered intracerebroventricularly to mice. As in the in vitro expts. the dose-response curve for the antagonist was shifted rightward in a parallel

fashion when D-serine was coinjected. This spectrum of activity displayed by a compound acting at the glycine binding site suggests that the therapeutic utility of glycine antagonists will be similar to those proposed for other types of glutamate receptor antagonists.

ST chlorokynurenate methylasprtate receptor glycine; anticonvulsant chlorokynurenate glutamate receptor

IT Anticonvulsants and Antiepileptics
(dichlorokynurenate as, methylaspartate receptors mediation of)

IT Receptors
RL: BIOL (Biological study)
(for methylaspartate, of brain, dichlorokynurenate effect on)

IT Brain, composition
(methylaspartate receptors of, dichlorokynurenate and glycine effect on)

IT Receptors
RL: BIOL (Biological study)
(glutamatergic, of brain, glycine-binding site of, dichlorokynurenate effect on)

IT Neurotransmission
(long-term potentiation, in hippocampus, dichlorokynurenate effect on)

IT 7665-99-8, CGMP
RL: BIOL (Biological study)
(accumulation of, by cerebellum, dichlorokynurenate effect on)

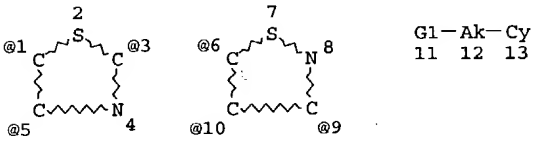
IT 131123-76-7
RL: BIOL (Biological study)
(methylaspartate receptor binding of glycine antagonism by)

IT 56-40-6, Glycine, biological studies
RL: BIOL (Biological study)
(methylaspartate receptor binding of, dichlorokynurenic antagonism of)

IT 51-41-2, Norepinephrine
RL: BIOL (Biological study)
(release of, by hippocampus, dichlorokynurenate and glycine effect on)

IT 7440-70-2, Calcium, biological studies
RL: BIOL (Biological study)
(transport of, by hippocampus, dichlorokynurenate effect on)

```
=> b reg
FILE 'REGISTRY' ENTERED AT 13:22:07 ON 17 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:   15 SEP 2004  HIGHEST RN 745743-57-1
DICTIONARY FILE UPDATES:  15 SEP 2004  HIGHEST RN 745743-57-1

TSCA INFORMATION NOW CURRENT THROUGH MAY 21, 2004

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d que stat l43
L19             STR
```




```
VAR G1=1/3/5/6/9/10
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
GGCAT   IS UNS  AT  12
GGCAT   IS UNS  AT  13
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC   1   6
NUMBER OF NODES IS  13

STEREO ATTRIBUTES: NONE
L27       14764 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GLUTAMATE RECEPTORS/CT
L28        2748 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L27 (L) METABOTROPIC
L29         878 SEA FILE=HCAPLUS ABB=ON  PLU=ON  RECEPTOR?/CW (L)GLUTAMATERGIC
                (L) METABOTROPIC
L30        3573 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L28 OR L29)
L31         217 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GLUTAMATE AGONISTS/CT
L32         172 SEA FILE=HCAPLUS ABB=ON  PLU=ON  NEUROTRANSMITTER AGONISTS+NT/C
                T (L) GLUTAMATERGIC
L33        1887 SEA FILE=HCAPLUS ABB=ON  PLU=ON  GLUTAMATE ANTAGONISTS/CT
L34       28926 SEA FILE=HCAPLUS ABB=ON  PLU=ON  NEUROTRANSMITTER ANTAGONISTS+N
                T/CT
L35        1183 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L34 (L) (GLUTAMATERGIC OR
                METHYL (1A) ASPARTATE)
L36        6600 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L30 OR L31 OR L32 OR L33 OR
                L35
L37             TRANSFER  PLU=ON  L36 1- RN :   51196 TERMS  (TERM LIMIT E
XCEE
                DED)
L38       51196 SEA FILE=REGISTRY ABB=ON  PLU=ON  L37
L39             TRANSFER  PLU=ON  L36 3878-6600 RN :   19902 TERMS
L40       19902 SEA FILE=REGISTRY ABB=ON  PLU=ON  L39
L41       67567 SEA FILE=REGISTRY ABB=ON  PLU=ON  L38 OR L40
L43         111 SEA FILE=REGISTRY SUB=L41 SSS FUL L19

100.0% PROCESSED    865 ITERATIONS                          111 ANSWERS
SEARCH TIME: 00.00.01


=> d his
```

```
     (FILE 'HOME' ENTERED AT 12:11:19 ON 17 SEP 2004)

     FILE 'HCAPLUS' ENTERED AT 12:11:26 ON 17 SEP 2004
                E COSFORD N/AU
L1           51 E4-9
                E MCDONALD I/AU
L2          171 E3-5,E16-19
                E HESS S/AU
L3          152 E3,E5,E46-49
                E VARNEY M/AU
L4           49 E3-4,E8-10
L5        30930 (SIBIA OR MERCK)/CS,PA
L6           34 L1-4 AND EXCIT?
L7            7 L6 AND AMINO (1A) ACID?

     FILE 'REGISTRY' ENTERED AT 12:18:22 ON 17 SEP 2004

     FILE 'HCAPLUS' ENTERED AT 12:18:35 ON 17 SEP 2004
L8              TRA L7 1- RN :      351 TERMS

     FILE 'REGISTRY' ENTERED AT 12:18:36 ON 17 SEP 2004
L9           351 SEA L8
L10           99 (NCSC2 OR NSC3)/ES AND L9
L11              STR
L12           50 L11
L13       613894 (NCSC2 OR NSC3)/ES
L14           50 L11 SAM SUB=L13
L15            0 ALKYNYLENE
L16              STR L11
L17              STR L16
L18           28 L17
L19              STR L11
L20           16 L19
L21              SCR 1839 AND 2021 AND 1992
L22              SCR 2039 OR 2050 OR 2048 OR 2053 OR 2052 OR 2043 OR 2054
L23              SCR 1645 AND 1783
L24              SCR 2103 AND 2106
L25           17 L19 AND L21 AND L23 OR L24 NOT L22
L26           20 L19 AND L21 AND L23 OR L24 NOT L22 SAM SUB=L13


     FILE 'HCAPLUS' ENTERED AT 13:01:46 ON 17 SEP 2004
                E METABOTROPIC/CT
                E E4+ALL
                E E2+ALL
                E E7+ALL
L27        14764 GLUTAMATE RECEPTORS/CT
L28         2748 L27 (L) METABOTROPIC
                E RECEPTORS/CT
L29          878 RECEPTOR?/CW (L)GLUTAMATERGIC (L) METABOTROPIC
L30         3573 L28-29
                E GLUTAMATE AGONISTS/CT
                E E3+ALL
L31          217 GLUTAMATE AGONISTS/CT
                E NEUROTRANSMITTER AGONISTS/CT
                E E3+ALL
L32          172 NEUROTRANSMITTER AGONISTS+NT/CT (L) GLUTAMATERGIC
                E  GLUTAMATE ANTAGONISTS/CT
                E E3+ALL
L33         1887 GLUTAMATE ANTAGONISTS/CT
                E NEUROTRANSMITTER ANTAGONISTS/CT
                E E3+ALL
L34        28926 NEUROTRANSMITTER ANTAGONISTS+NT/CT
L35         1183 L34 (L) (GLUTAMATERGIC OR METHYL (1A) ASPARTATE)
L36         6600 L30 OR L31 OR L32 OR L33 OR L35

     FILE 'REGISTRY' ENTERED AT 13:08:34 ON 17 SEP 2004

     FILE 'HCAPLUS' ENTERED AT 13:08:37 ON 17 SEP 2004

     FILE 'REGISTRY' ENTERED AT 13:11:03 ON 17 SEP 2004
L37             TRA L36 1- RN :    51196 TERMS

     FILE 'REGISTRY, REGISTRY' ENTERED AT 13:11:04 ON 17 SEP 2004
L38        51196 SEA L37
```

```
     FILE 'HCAPLUS' ENTERED AT 13:13:23 ON 17 SEP 2004
L39             TRA L36 3878-6600 RN :    19902 TERMS

     FILE 'REGISTRY' ENTERED AT 13:14:50 ON 17 SEP 2004
L40         19902 SEA L39
L41         67567 L38 OR L40
L42             5 L19 SAM SUB=L41
L43           111 L19 FULL SUB=L41
                  SAVE TEMP CHOI135F0/A L42
                  SAVE TEMP CHOI135F0/A L43

     FILE 'HCAPLUS' ENTERED AT 13:17:27 ON 17 SEP 2004
L44            39 L43

     FILE 'HCAOLD' ENTERED AT 13:17:37 ON 17 SEP 2004
L45             0 L43

     FILE 'HCAPLUS' ENTERED AT 13:17:45 ON 17 SEP 2004
L46           121 L5 AND L36
L47            44 L1-4 AND L36
L48             7 L44 AND L1-5
L49            32 L44 NOT L48
L50            21 L49 AND (PY<=1999 OR AY<=1999 OR PRY<=1999 OR AD<19990831 OR PD
L51             2 L50 AND L36
L52            19 L50 NOT L51

=> b hcap
FILE 'HCAPLUS' ENTERED AT 13:22:54 ON 17 SEP 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)


Copyright of the articles to which records in this database refer is
held by the publishers listed in the PUBLISHER (PB) field (available
for records published or updated in Chemical Abstracts after December
26, 1996), unless otherwise indicated in the original publications.
The CA Lexicon is the copyrighted intellectual property of the
the American Chemical Society and is provided to assist you in searching
databases on STN.  Any dissemination, distribution, copying, or storing
of this information, without the prior written consent of CAS, is
strictly prohibited.

FILE COVERS 1907 - 17 Sep 2004  VOL 141 ISS 13
FILE LAST UPDATED: 16 Sep 2004  (20040916/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


=> d all fhitstr l48 tot

L48  ANSWER 1 OF 7  HCAPLUS  COPYRIGHT 2004 ACS on STN
AN   2004:523298  HCAPLUS
DN   141:133562
ED   Entered STN:  30 Jun 2004
TI   5-[(2-Methyl-1,3-thiazol-4-yl)ethynyl]-2,3'-bipyridine: a highly potent,
     orally active metabotropic glutamate subtype 5 (mGlu5) receptor antagonist
     with anxiolytic activity
AU   Roppe, Jeffrey R.; Wang, Bowei; Huang, Dehua; Tehrani, Lida; Kamenecka,
     Theodore; Schweiger, Edwin J.; Anderson, Jeffery J.; Brodkin, Jesse;
     Jiang, Xiaohui; Cramer, Merryl; Chung, Janice; Reyes-Manalo, Grace; Munoz,
     Benito; Cosford, Nicholas D. P.
CS   Department of Medicinal Chemistry, Merck Research Laboratories,
     San Diego, CA, 92121, USA
SO   Bioorganic & Medicinal Chemistry Letters (2004), 14(15), 3993-3996
     CODEN: BMCLE8; ISSN: 0960-894X
PB   Elsevier Science B.V.
DT   Journal
LA   English
CC   1-3 (Pharmacology)
     Section cross-reference(s): 28
AB   Structure-activity relation studies leading to the discovery of a new,
     orally active mGlu5 receptor antagonist are described.  The title compound,
     5-[(2-methyl-1,3-thiazol-4-yl)ethynyl]-2,3'-bipyridine, is highly potent
```

in vitro, has good in vivo receptor occupancy, and is efficacious in the rat fear-potentiated startle model of anxiety following oral dosing.

ST methylthiazolylbipyridine deriv mGlu5 antagonist anxiolytic; metabotropic glutamate antagonist ethynylbipyridine deriv

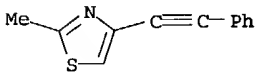
IT **329203-01-2P 329204-16-2P 329204-25-3P**
329204-27-5P 329205-68-7P 497145-23-0P
497145-24-1P 722453-33-0P 727428-69-5P 727428-70-8P
727428-71-9P 727428-72-0P 727428-73-1P 727428-74-2P 727428-75-3P
727428-76-4P 727428-77-5P 727428-78-6P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and structure activity relations of [(methylthiazolyl)ethynyl]bipyridines as potent, orally active metabotropic glutamate subtype 5 receptor antagonist with anxiolytic activity)

IT 329203-85-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and structure activity relations of [(methylthiazolyl)ethynyl]bipyridines as potent, orally active metabotropic glutamate subtype 5 receptor antagonist with anxiolytic activity)

IT 69045-79-0P **329204-13-9P 329204-97-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and structure activity relations of [(methylthiazolyl)ethynyl]bipyridines as potent, orally active metabotropic glutamate subtype 5 receptor antagonist with anxiolytic activity)

IT **329203-01-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and structure activity relations of [(methylthiazolyl)ethynyl]bipyridines as potent, orally active metabotropic glutamate subtype 5 receptor antagonist with anxiolytic activity)

RN 329203-01-2 HCAPLUS
CN Thiazole, 2-methyl-4-(phenylethynyl)- (9CI) (CA INDEX NAME)



L48 ANSWER 2 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2004:371151 HCAPLUS
DN 140:391275
ED Entered STN: 07 May 2004
TI Preparation of isotopically labeled heterocyclic alkyne derivatives as tracers for metabotropic glutamate receptor binding
IN **Cosford, Nicholas David Peter**; Govek, Steven Patrick; Hamill, Terence Gerard; Kamenecka, Theodore; Roppe, Jeffrey Roger; Seiders, Thomas Jonathan
PA **Merck** & Co., Inc., USA
SO PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM G01N
CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 8

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004038374	A2	20040506	WO 2003-US33613	20031024

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,

CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

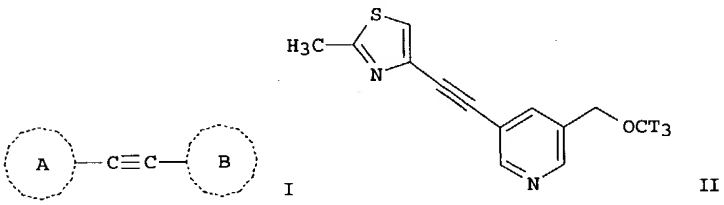
PRAI US 2002-420809P P 20021024

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2004038374	ICM	G01N

OS MARPAT 140:391275

GI



AB The present invention is directed to isotopically labeled alkyne derivative compds. I (A = optionally substituted heterocycle; B = optionally substituted aryl, heterocycle, C3-20 cycloalkyl, C3-20 cycloalkyneyl, C3-20 cycloalkadienyl, C3-20 cycloalkatrienyl, C3-2- cycloalkynyl, C3-20 cycloalkadiynyl; except when A = 6-methyl-2-pyridyl then B cannot = 3-MeOC6H4 or Ph) wherein the compound is isotopically labeled with at least one 11C, 13C,14C, 18F, 15O, 13N, 35S, 2H, or 3H atom. In particular, the present invention is directed to 11C, 13C, 14C, 18F, 15O, 13N, 35S, 2H, and 3H labeled heterocyclic alkynes and methods of their preparation The present invention further includes a method of use of the 11C, 18F, 15O, or 13N labeled heterocyclic alkyne compds. as tracers in positron emission tomog. (PET) imaging, particularly in the study of metabolic conditions in mammals, specifically conditions modulated by metabotropic glutamate receptors subtype 5 (mGluR5). Thus, Pd-catalyzed coupling of (5-bromopyridin-3-yl)methanol (preparation given) with 2-methyl-4-(trimethylsilylethynyl)-1,3-thiazole, followed by methylation with 11CH3I gave tritiated hetercyclic alkyne II. II was tested for in vitro binding of mGlu5 receptor protein.

ST isotopically labeled heterocyclic alkyne prepn; metabotropic glutamate receptor binding labeled heterocyclic alkyne prepn; positron emission tomog labeled heterocyclic alkyne prepn

IT Alkynes
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(heterocyclic, isotopically labeled; preparation of isotopically labeled heterocyclic alkyne derivs. as tracers for metabotropic glutamate receptor binding)

IT Glutamate receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metabotropic; preparation of isotopically labeled heterocyclic alkyne derivs. as tracers for metabotropic glutamate receptor binding)

IT Positron-emission tomography
(preparation of isotopically labeled heterocyclic alkyne derivs. as tracers for metabotropic glutamate receptor binding)

IT **686767-95-3P 686768-37-6P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of isotopically labeled heterocyclic alkyne derivs. as tracers for metabotropic glutamate receptor binding)

IT **524924-79-6P** 524924-80-9P **686767-96-4P**
686767-97-5P 686767-98-6P 686767-99-7P 686768-01-4P
686768-02-5P 686768-04-7P 686768-06-9P
686768-10-5P 686768-13-8P 686768-15-0P
686768-17-2P **686768-19-4P 686768-25-2P**
686768-27-4P 686768-29-6P 686768-30-9P
686768-31-0P 686768-32-1P 686768-33-2P
686768-35-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

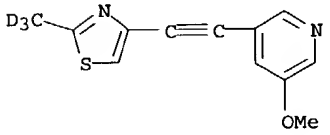
(preparation of isotopically labeled heterocyclic alkyne derivs. as tracers for metabotropic glutamate receptor binding)

IT 62-55-5, Thioacetamide 109-09-1, 2-Chloropyridine 625-92-3, 3,5-Dibromopyridine 661-69-8, Hexamethylditin 774-53-8 1066-54-2, Trimethylsilylacetylene 1120-90-7, 3-Iodopyridine 1611-92-3, 1,3-Dibromo-5-methylbenzene 1945-84-2, 2-Ethynylpyridine 4175-77-3, 2,4-Dibromothiazole 14630-40-1, Bis(trimethylsilyl)acetylene 20826-04-4, 5-Bromonicotinic acid 52753-63-6, reactions 73183-34-3 74094-67-0, Chloroacetyl chloride, 1-14C 97165-77-0, 3,5-Dibromobenzonitrile 179898-34-1, 3-Bromo-5-fluorobenzonitrile 329203-85-2 **329204-97-9** 444120-91-6 **686768-41-2** **686768-43-4** 686768-44-5 686768-45-6 686768-46-7 **686768-47-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of isotopically labeled heterocyclic alkyne derivs. as tracers for metabotropic glutamate receptor binding)

IT 37669-64-0P, (5-Bromopyridin-3-yl)methanol 50720-12-2P, 3-Bromo-5-methoxypyridine 124289-21-0P, 3-Bromo-5-methylbenzonitrile **524924-75-2P** 524924-76-3P **524924-81-0P** 524924-82-1P 686768-21-8P 686768-23-0P **686768-48-9P** **686768-49-0P** 686768-50-3P 686768-51-4P **686768-52-5P** **686768-53-6P** **686768-54-7P** **686768-55-8P** **686768-56-9P** **686768-57-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of isotopically labeled heterocyclic alkyne derivs. as tracers for metabotropic glutamate receptor binding)

IT **686767-95-3P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of isotopically labeled heterocyclic alkyne derivs. as tracers for metabotropic glutamate receptor binding)

RN 686767-95-3 HCAPLUS
CN Pyridine, 3-methoxy-5-[[2-(methyl-d3)-4-thiazolyl]ethynyl]- (9CI) (CA INDEX NAME)



L48 ANSWER 3 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:222367 HCAPLUS
DN 138:238175
ED Entered STN: 21 Mar 2003
TI Preparation of heterocyclic compounds as metabotropic glutamate receptor 5 (mGluR5) modulators
IN **Cosford, Nicholas David Peter**; Bleicher, Leo Solomon; Vernier, Jean-Michel Andre; Cube, Rowena V.; Schweiger, Edwin J.; **McDonald, Ian**
PA **Merck** & Co., Inc., USA
SO U.S. Pat. Appl. Publ., 20 pp., Cont.-in-part of U.S. Ser. No. 387,073, abandoned.
CODEN: USXXCO
DT Patent
LA English
IC ICM C07D279-12
ICS C07D241-02
NCL 544059000; 544336000; 544063000; 534751000
CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 2

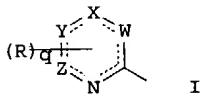
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003055247	A1	20030320	US 2002-217800	20020813
	US 6774138	B2	20040810		
PRAI	US 1999-387073	B2	19990831		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES

US 2003055247 ICM C07D279-12
ICS C07D241-02
NCL 544059000; 544336000; 544063000; 534751000
US 2003055247 ECLA C07D213/16; C07D213/30B; C07D239/26B; C07D241/12C; C07D249/08; C07D263/32; C07D271/06B; C07D077/22C; C07D277/24; C07D277/40; C07D285/00B3; C07D333/08

OS MARPAT 138:238175
GI



I

AB The title compds. with general formula of A-L-B [wherein A = 5-7 membered ring I (where at least one of W, X, Y, and Z = (CR)p; p = 0-2; and the remainder of W, X, Y, and Z = independently O, N, S; R = halo, SH, NO2, CO2H, carbamate, carboxamide, OH, ester, CN, NH2, amide, amidine, amido, SO2, (un)substituted hydrocarbyl, aryl, or heterocyclyl); q = 0-3; L = (un)substituted alkenylene, alkynylene, or azo; B = (un)substituted (cyclo)hydrocarbyl, heterocyclyl, or aryl] and enantiomers, diastereomers, mixts., or their pharmaceutically acceptable salts thereof, which are capable of modulating the activity of excitatory amino acid receptors such as metabotropic glutamate receptor, are prepared Thus, reacting 2-bromo-1,3-thiazole with phenylacetylene in the presence of CuI, Et3N, and PdCl2(PPh3)2 in DME, followed by treatment of the resulting 2-(phenylethynyl)-1,3-thiazole with p-TsOH afforded 2-(phenylethynyl)-1,3-thiazole, p-TsOH salt.

ST heterocycle thiazole prepn metabotropic glutamate receptor modulator analgesic

IT Amino acid receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(excitatory; preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

IT Glutamate receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metabotropic; preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

IT 329202-67-7P 329202-70-2P **329202-84-8P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

IT **329202-19-9P** 329202-20-2P **329202-23-5P** 329202-24-6P
329202-25-7P 329202-26-8P **329202-27-9P** 329202-28-0P
329202-29-1P **329202-30-4P** 329202-31-5P **329202-32-6P**
329202-33-7P 329202-34-8P 329202-35-9P 329202-36-0P 329202-37-1P
329202-38-2P 329202-40-6P 329202-42-8P 329202-44-0P 329202-46-2P
329202-48-4P 329202-50-8P 329202-52-0P 329202-54-2P 329202-56-4P
329202-58-6P 329202-61-1P 329202-64-4P 329202-73-5P
329202-79-1P 329202-80-4P 329202-83-7P
329202-87-1P 329202-90-6P 329205-94-9P 329205-96-1P 329205-98-3P
329206-00-0P 329206-02-2P 329206-04-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

IT 78-93-3, 2-Butanone, reactions 108-50-9, 2,6-Dimethylpyrazine 115-19-5, 2-Methyl-3-butyne-2-ol 456-48-4, 3-Fluorobenzaldehyde 464-49-3 497-38-1, Norcamphor 502-42-1, Cycloheptanone 502-49-8, Cyclooctanone 536-74-3, Phenylacetylene 589-92-4, 4-Methylcyclohexanone 626-55-1, 3-Bromopyridine 627-19-0, 1-Pentyne 627-41-8, Methyl propargyl ether 917-92-0, 3,3-Dimethyl-1-butyne 931-48-6, Cyclohexylethyne 931-49-7, 1-Ethynylcyclohexene 1066-54-2, Trimethylsilylacetylene 1072-72-6, Tetrahydrothiopyran-4-one 1757-42-2, 3-Methylcyclopentanone 1945-84-2, 2-Ethynylpyridine 2320-30-1, 3,5-Dimethylcyclohexanone 2816-57-1, 2,6-Dimethylcyclohexanone 3034-48-8, 2-Bromo-5-nitro-1,3-thiazole 3034-53-5, 2-Bromo-1,3-thiazole 5315-25-3, 2-Bromo-6-methylpyridine 13223-25-1, 2-Chloro-4,6-dimethoxypyrimidine 13368-65-5 14376-79-5, 3,3,5,5-Tetramethylcyclohexanone 17356-19-3, 1-Ethynylcyclopentanol

17715-00-3, 3-Cyclohexyl-1-propyne 29943-42-8, Tetrahydro-4H-pyran-4-one
74115-12-1, 5-Chloro-3-pyridinol 111196-81-7, 2-Chloro-5-ethylpyrimidine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

IT 2510-23-8P 24202-80-0P 150145-19-0P 329202-21-3P 329202-22-4P 329202-76-8P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD

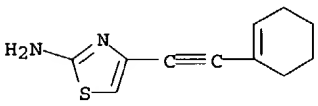
RE
(1) Anon; WO 9603406 1996 HCAPLUS
(2) Anon; WO 9902497 1999
(3) Anon; WO 0116121 2001 HCAPLUS
(4) Gasparini, F; Brit. J. Pharmacology 1999, V249
(5) Shih, C; J. Med. Chem. 1992, V35, P1109 HCAPLUS
(6) Trybulski; US 4990520 A 1991 HCAPLUS
(7) Varney, M; Brit. J. Pharmacology 1999, V126(Supp), P248
(8) Varney, M; J. Med. Chem. 1997, V40, P2502 HCAPLUS
(9) Varney, M; J. Pharmacology and Exptl. Therapeutics 1999, V290, P170 HCAPLUS

IT **329202-84-8P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

RN 329202-84-8 HCAPLUS
CN 2-Thiazolamine, 4-(1-cyclohexen-1-ylethynyl)-, 4-methylbenzenesulfonate (9CI) (CA INDEX NAME)

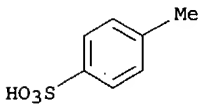
CM 1

CRN 329202-83-7
CMF C11 H12 N2 S



CM 2

CRN 104-15-4
CMF C7 H8 O3 S



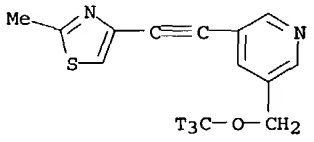
L48 ANSWER 4 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2003:91263 HCAPLUS
DN 138:379345
ED Entered STN: 06 Feb 2003
TI [3H]-Methoxymethyl-MTEP and [3H]-Methoxy-PEPy: potent and selective radioligands for the metabotropic glutamate subtype 5 (mGlu5) receptor
AU **Cosford, Nicholas D. P.**; Roppe, Jeffrey; Tehrani, Lida; Schweiger, Edwin J.; Seiders, T. Jon; Chaudary, Ashok; Rao, Sara; **Varney, Mark A.**
CS Department of Chemistry, **Merck** Research Laboratories, San Diego, CA, 92121, USA
SO Bioorganic & Medicinal Chemistry Letters (2003), 13(3), 351-354
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier Science Ltd.
DT Journal
LA English

CC 2-1 (Mammalian Hormones)
Section cross-reference(s): 8
AB The design, synthesis, and characterization of two potent, non-competitive radioligands, [3H]-methoxymethyl-MTEP and [3H]-methoxy-PEPy, that are selective for the mGlu5 receptor are described.
ST glutamate mGluR5 receptor antagonist radioligand brain rat
IT Brain
([3H]-Methoxymethyl-MTEP and [3H]-Methoxy-PEPy in relation to design, synthesis and in-vitro characterization in rat brain membranes of potent and selective radioligands for metabotropic glutamate subtype-5 receptor)
IT Glutamate receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metabotropic, mGluR5; [3H]-Methoxymethyl-MTEP and [3H]-Methoxy-PEPy in relation to design, synthesis and in-vitro characterization in rat brain membranes of potent and selective radioligands for metabotropic glutamate subtype-5 receptor)
IT Ligands
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(radioligands; [3H]-Methoxymethyl-MTEP and [3H]-Methoxy-PEPy in relation to design, synthesis and in-vitro characterization in rat brain membranes of potent and selective radioligands for metabotropic glutamate subtype-5 receptor)
IT **524924-79-6P** 524924-80-9P
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
([3H]-Methoxymethyl-MTEP and [3H]-Methoxy-PEPy in relation to design, synthesis and in-vitro characterization in rat brain membranes of potent and selective radioligands for metabotropic glutamate subtype-5 receptor)
IT 96206-92-7P 219914-59-7P **329205-68-7P 524924-75-2P**
524924-76-3P 524924-77-4P **524924-78-5P**
RL: BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
([3H]-Methoxymethyl-MTEP and [3H]-Methoxy-PEPy in relation to design, synthesis and in-vitro characterization in rat brain membranes of potent and selective radioligands for metabotropic glutamate subtype-5 receptor)
IT 37669-64-0P 50720-12-2P 173999-17-2P **329204-97-9P**
524924-81-0P 524924-82-1P
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
([3H]-Methoxymethyl-MTEP and [3H]-Methoxy-PEPy in relation to design, synthesis and in-vitro characterization in rat brain membranes of potent and selective radioligands for metabotropic glutamate subtype-5 receptor)
IT 625-92-3 1945-84-2 29681-44-5 329203-85-2
RL: RCT (Reactant); RACT (Reactant or reagent)
([3H]-Methoxymethyl-MTEP and [3H]-Methoxy-PEPy in relation to design, synthesis and in-vitro characterization in rat brain membranes of potent and selective radioligands for metabotropic glutamate subtype-5 receptor)
RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anderson, J; J Pharmacol Exp Ther in press
(2) Brodkin, J; Pharmaco, Biochem Behav 2002, V73, P359 HCAPLUS
(3) Chiamulera, C; Nat Neurosci 2001, V4, P873 HCAPLUS
(4) Cosford, N; J Med Chem in press
(5) Daggett, L; Neuropharmacology 1995, V34, P871 HCAPLUS
(6) Gasparini, F; Bioorg Med Chem Lett 2002, V12, P407 HCAPLUS
(7) Klodzinska, A; Pol J Pharmacol 2000, V52, P463 HCAPLUS
(8) Patel, S; Life Sci in press
(9) Pin, J; Current drug targets: CNS Neurol Disord 2002, V1, P297 HCAPLUS
(10) Schulz, B; Neuropharmacology 2001, V41, P1 HCAPLUS
(11) Spooren, W; Eur J Pharmacol 2002, V435, P161 HCAPLUS
(12) Spooren, W; J Pharmacol Exp Ther 2000, V295, P1267 HCAPLUS
(13) Tatarczynska, E; Br J Pharmacol 2001, V132, P1423 HCAPLUS
(14) Varney, M; Current drug targets: CNS Neurol Disord 2002, V1, P283 HCAPLUS
(15) Varney, M; Drug Discov Today: HTS Suppl 2000, V1, P20 HCAPLUS
(16) Varney, M; J Pharmacol Exp Ther 1999, V290, P170 HCAPLUS
IT **524924-79-6P**
RL: ARG (Analytical reagent use); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); ANST (Analytical study);

BIOL (Biological study); PREP (Preparation); USES (Uses)
([3H]-Methoxymethyl-MTEP and [3H]-Methoxy-PEPy in relation to design, synthesis and in-vitro characterization in rat brain membranes of potent and selective radioligands for metabotropic glutamate subtype-5 receptor)

RN 524924-79-6 HCAPLUS

CN Pyridine, 3-(methoxy-t3-methyl)-5-[(2-methyl-4-thiazolyl)ethynyl]- (9CI) (CA INDEX NAME)



L48 ANSWER 5 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 2002:943427 HCAPLUS

DN 138:170117

ED Entered STN: 13 Dec 2002

TI 3-[(2-Methyl-1,3-thiazol-4-yl)ethynyl]- pyridine: A Potent and Highly Selective Metabotropic Glutamate Subtype 5 Receptor Antagonist with Anxiolytic Activity

AU **Cosford, Nicholas D. P.**; Tehrani, Lida; Roppe, Jeffrey; Schweiger, Edwin; Smith, Nicholas D.; Anderson, Jeffrey; Bristow, Linda; Brodkin, Jesse; Jiang, Xiaohui; **McDonald, Ian**; Rao, Sara; Washburn, Mark; **Varney, Mark A.**

CS **Merck** Research Laboratories, San Diego, CA, 92121, USA

SO Journal of Medicinal Chemistry (2003), 46(2), 204-206
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

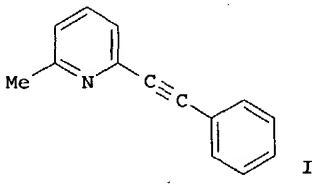
DT Journal

LA English

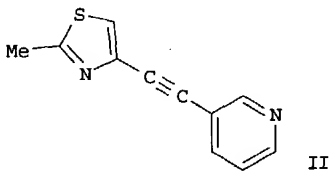
CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

OS CASREACT 138:170117

GI



I



II

AB 2-Methyl-6-(phenylethynyl)pyridine (I), a potent noncompetitive mGlu5 receptor antagonist widely used to characterize the pharmacol. of mGlu5 receptors, suffers from a number of shortcomings as a therapeutic agent, including off-target activity and poor aqueous solubility Seeking to improve the properties of I led to the synthesis of compound II, a highly selective mGlu5 receptor antagonist that is 5-fold more potent than I in the rat fear-potentiated startle model of anxiety.

ST thiazole pyridinylethynylmethyl prepn glutamate receptor antagonist

IT Nervous system, disease
(central; preparation and mGlu5 receptor antagonistic activity of phenyl- and pyridinylethynylthiazoles)

IT Structure-activity relationship
(glutamatergic antagonist; preparation and mGlu5 receptor antagonistic activity of phenyl- and pyridinylethynylthiazoles)

IT Glutamate receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metabotropic, mGluR5; preparation and mGlu5 receptor antagonistic activity of phenyl- and pyridinylethynylthiazoles)

IT Blood-brain barrier
Human
Nervous system agents
(preparation and mGlu5 receptor antagonistic activity of phenyl- and pyridinylethynylthiazoles)

IT 109-04-6, 2-Bromopyridine 591-50-4, Iodobenzene 626-55-1, 3-Bromopyridine 1120-87-2, 4-Bromopyridine
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and mGlu5 receptor antagonist activity of phenyl- and pyridinylethynylthiazoles via coupling reactions of halobenzene or halopyriidnes with Me[(trimethylsilyl)ethynyl]thiazole)

IT 536-74-3, Phenylacetylene 3034-53-5, 2-Bromo-1,3-thiazole 4175-77-3, 2,4-Dibromothiazole 34259-99-9, 4-Bromo-1,3-thiazole
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation and mGlu5 receptor antagonist activity of phenylethynylthiazoles via coupling reactions of bromothiazoles and phenylacetylene)

IT **329203-16-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and mGlu5 receptor antagonist activity of phenylethynylthiazoles via coupling reactions of bromothiazoles and phenylacetylene)

IT **329203-13-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and mGlu5 receptor antagonist activity of phenylethynylthiazoles via coupling reactions of bromothiazoles and phenylacetylene)

IT 594-27-4 51364-51-3
RL: MSC (Miscellaneous)
(preparation and mGlu5 receptor antagonistic activity of phenyl- and pyridinylethynylthiazoles)

IT 62-55-5, Thioacetamide 14630-40-1, Bis(trimethylsilyl)acetylene
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of methyl[(trimethylsilyl)ethynyl]thiazole via cyclocondensation of thioacetamide with intermediate chloro(trimethylsilyl)butynone obtained by acetylation of chloroacetylchloride with bis(trimethylsilyl)acetylene)

IT 18245-82-4P 329203-85-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of methyl[(trimethylsilyl)ethynyl]thiazole via cyclocondensation of thioacetamide with intermediate chloro(trimethylsilyl)butynone obtained by acetylation of chloroacetylchloride with bis(trimethylsilyl)acetylene)

IT **329203-01-2P 329205-68-7P 497145-23-0P 497145-24-1P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, structure-activity relationship, and mGlu5 receptor antagonist activity of phenyl- and pyridinylethynylthiazoles via coupling reactions of halobenzene or halopyriidnes with Me[(trimethylsilyl)ethynyl]thiazole)

IT **35070-01-0P**
RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation, structure-activity relationship, and mGlu5 receptor antagonist activity of phenylethynylthiazoles via coupling reactions of bromothiazoles and phenylacetylene)

IT **111600-88-5P 497145-22-9P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, structure-activity relationship, and mGlu5 receptor antagonist activity of phenylethynylthiazoles via coupling reactions of bromothiazoles and phenylacetylene)

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD

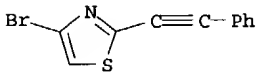
RE

(1) Anderson, J; J Pharmacol Exp Ther, in press
(2) Brauener-Osborne, H; J Med Chem 2000, V43, P2609
(3) Brodkin, J; Pharmacol, Biochem Behav 2002, V73, P359 HCAPLUS
(4) Chiamulera, C; Nat Neurosci 2001, V4, P873 HCAPLUS
(5) Conn, P; Annu Rev Pharmacol Toxicol 1997, V37, P205 HCAPLUS
(6) Cosford, N; Bioorg Med Chem Lett, in press
(7) Daggett, L; Neuropharmacology 1995, V34, P871 HCAPLUS
(8) Gasparini, F; Curr Opin Pharmacol 2002, V2, P43 HCAPLUS
(9) Gasparini, F; Neuropharmacology 1999, V38, P1493 HCAPLUS
(10) Klodzinska, A; Pol J Pharmacol 2000, V52, P463 HCAPLUS
(11) Movsesyan, V; J Pharmacol Exp Ther 2001, V296, P41 HCAPLUS
(12) Ozawa, S; Prog Neurobiol (Oxford) 1998, V54, P581 HCAPLUS
(13) O'Leary, D; Br J Pharmacol 2000, V131, P1429 HCAPLUS

(14) Pin, J; Curr Drug Targets:CNS Neurol Disord 2002, V1, P297 HCAPLUS
(15) Schulz, B; Neuropharmacology 2001, V41, P1 HCAPLUS
(16) Spooren, W; Eur J Pharmacol 2002, V435, P161 HCAPLUS
(17) Spooren, W; J Pharmacol Exp Ther 2000, V295, P1267 HCAPLUS
(18) Tatarczynska, E; Br J Pharmacol 2001, V132, P1423 HCAPLUS
(19) Varney, M; Curr Drug Targets:CNS Neurol Disord 2002, V1, P283 HCAPLUS
(20) Varney, M; Drug Discovery Today:HTS Suppl 2000, V1, P20 HCAPLUS
(21) Varney, M; J Pharmacol Exp Ther 1999, V290, P170 HCAPLUS

IT **329203-16-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and mGlu5 receptor antagonist activity of phenylethynylthiazoles via coupling reactions of bromothiazoles and phenylacetylene)

RN 329203-16-9 HCAPLUS
CN Thiazole, 4-bromo-2-(phenylethynyl)- (9CI) (CA INDEX NAME)

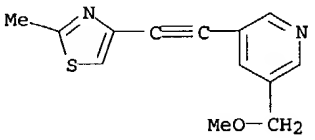


L48 ANSWER 6 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:932568 HCAPLUS
DN 138:379544
ED Entered STN: 10 Dec 2002
TI [3H]methoxymethyl-3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine binding to metabotropic glutamate receptor subtype 5 in rodent brain: in vitro and in vivo characterization
AU Anderson, Jeffery J.; Rao, Sara P.; Rowe, Blake; Giracello, Darlene R.; Holtz, Greg; Chapman, Deborah F.; Tehrani, Lida; Bradbury, Margaret J.; **Cosford, Nicholas D. P.; Varney, Mark A.**
CS Department of Neuropharmacology, **Merck** Research Laboratories, San Diego, CA, USA
SO Journal of Pharmacology and Experimental Therapeutics (2002), 303(3), 1044-1051
CODEN: JPETAB; ISSN: 0022-3565
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
CC 2-8 (Mammalian Hormones)
Section cross-reference(s): 1
AB The binding of [3H]methoxymethyl-3-[(2-methyl-1,3-thiazol-4-yl)ethynyl]pyridine (methoxymethyl-MTEP), a potent and selective antagonist for metabotropic glutamate (mGlu)5 receptors, was characterized in rat brain both in vitro and in vivo. Non-specific binding, as defined with 10 .mu.M 2-methyl-6-(phenylethynyl)-pyridine (MPEP), was less than 10% of total binding in rat brain membranes. The binding of [3H]methoxymethyl-MTEP was of high affinity (Kd = 20.+-.2.7 nM), saturable (Bmax = 487.+-.48 fmol/mg protein), and to a single site. The mGlu5 antagonists methoxymethyl-MTEP and MPEP displaced [3H]methoxymethyl-MTEP binding with IC50 values of 30 and 15 nM, resp. In vivo administration of [3H]methoxymethyl-MTEP (50 .mu.Ci/kg i.v.) revealed 12-fold higher binding in hippocampus (an area enriched in mGlu5 receptors) relative to cerebellum (an area with few mGlu5 receptors) in rats. Similarly, administration of [3H]methoxymethyl-MTEP to mGlu5-deficient mice demonstrated binding at background levels in forebrain, whereas wild-type littermates exhibited 17-fold higher binding in forebrain relative to cerebellum. Systemic administration of unlabeled mGlu5 antagonists methoxymethyl-MTEP and MPEP to rats reduced the binding of [3H]methoxymethyl-MTEP with ID50 values of 0.8 and 2 mg/kg i.p., resp., 1 h post-treatment. The mGlu5 agonist 2-chloro-5-hydroxyphenylglycine (CHPG) (0.3, 1, and 3 .mu.mol) dose-dependently increased phosphoinositide (PI) hydrolysis in the hippocampus after i.c.v. administration in rats. CHPG-evoked increases in PI hydrolysis were blocked with MPEP at a dose (10 mg/kg i.p.) that markedly reduced [3H]methoxymethyl-MTEP binding in vivo. These results indicate that [3H]methoxymethyl-MTEP is a selective radioligand for labeling mGlu5 and is useful for studying the binding of mGlu5 receptors in rat brain in vitro and in vivo.
ST methoxymethyl methyl thiazol yl ethynyl pyridine binding mGLUR5 brain
IT Brain
(cerebellum; methoxymethyl-MTEP binds to mGluR5 and is a useful tool for studying mGlu5 receptor function/signaling in rodent brain)
IT Brain

(forebrain; methoxymethyl-MTEP binds to mGluR5 and is a useful tool for studying mGlu5 receptor function/signaling in rodent brain)
IT Brain
(hippocampus; methoxymethyl-MTEP binds to mGluR5 and is a useful tool for studying mGlu5 receptor function/signaling in rodent brain)
IT Transgene
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mGluR5 deficiency mice; methoxymethyl-MTEP binds to mGluR5 and is a useful tool for studying mGlu5 receptor function/signaling in rodent brain)
IT Glutamate receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(metabotropic, mGluR5; methoxymethyl-MTEP binds to mGluR5 in rodent brain membrane and is a useful tool for studying mGlu5 receptor function/signaling in rodent brain)
IT Phosphatidylinositols
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(methoxymethyl-MTEP binds to mGluR5 and is a useful tool for studying mGlu5 receptor function/signaling in rodent brain)
IT Cell membrane
(methoxymethyl-MTEP binds to mGluR5 in rodent brain membrane and is a useful tool for studying mGlu5 receptor function/signaling in rodent brain)
IT 170846-74-9
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mGlu5 agonist; methoxymethyl-MTEP binds to mGluR5 and is a useful tool for studying mGlu5 receptor function/signaling in rodent brain)
IT 96206-92-7, MPEP
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mGluR5 antagonist; methoxymethyl-MTEP binds to mGluR5 and is a useful tool for studying mGlu5 receptor function/signaling in rodent brain)
IT **528602-22-4**
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(methoxymethyl-MTEP binds to mGluR5 and is a useful tool for studying mGlu5 receptor function/signaling in rodent brain)
IT 56-86-0, L-Glutamic acid, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(methoxymethyl-MTEP binds to mGluR5 and is a useful tool for studying mGlu5 receptor function/signaling in rodent brain)
RE.CNT 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Atack, J; Neuropsychopharmacology 1999, V20, P255 HCAPLUS
(2) Bordi, F; Brain Res 2000, V871, P223 HCAPLUS
(3) Brodkin, J; Pharmacol Biochem Behav 2002, V73, P359 HCAPLUS
(4) Conn, P; Annu Rev Pharmacol Toxicol 1997, V37, P205 HCAPLUS
(5) Cosford, N; Bioorg Med Chem Lett, in press 2002
(6) Fisher, K; Neuroreport 1996, V7, P2743 HCAPLUS
(7) Fisher, K; Neuroreport 1998, V9, P1169 HCAPLUS
(8) Freedman, S; Eur J Pharmacol 1989, V174, P253 HCAPLUS
(9) Gasparini, F; Bioorg Med Chem Lett 2002, V12, P407 HCAPLUS
(10) Gasparini, F; Neuropharmacology 1999, V38, P1493 HCAPLUS
(11) Goeders, N; Life Sci 1985, V37, P345 HCAPLUS
(12) Jia, H; J Comp Neurol 1999, V410, P627 HCAPLUS
(13) Johnson, M; Brain Res 1999, V821, P539 HCAPLUS
(14) Karim, F; J Neurosci 2001, V21, P3771 HCAPLUS
(15) Laemmli, U; Nature (Lond) 1970, V227, P680 HCAPLUS
(16) Laporte, A; Eur J Pharmacol 1994, V271, P505 HCAPLUS
(17) Lu, Y; J Neurosci 1997, V17, P5196 HCAPLUS
(18) Martin, L; Neuron 1992, V9, P259 HCAPLUS
(19) Murray, F; Eur J Pharmacol 2000, V397, P263 HCAPLUS
(20) Mutel, V; J Neurochem 1998, V71, P2558 HCAPLUS
(21) Mutel, V; J Neurochem 2000, V75, P2590 HCAPLUS
(22) Nakanishi, S; Clin Neuropharmacol 1992, V15(Suppl 1), P4A
(23) O'Leary, D; Br J Pharmacol 2000, V131, P1429 HCAPLUS
(24) Pagano, A; J Biol Chem 2000, V275, P33750 HCAPLUS
(25) Patel, S; Eur J Pharmacol 1994, V267, P329 HCAPLUS
(26) Paxinos, G; The Rat Brain in Stereotaxic Coordinates 1986
(27) Pin, J; Neuropharmacology 1995, V34, P1 HCAPLUS
(28) Ransom, R; J Neurochem 1988, V51, P830 HCAPLUS
(29) Romano, C; J Comp Neurol 1995, V355, P455 HCAPLUS
(30) Schaffhauser, H; Mol Pharmacol 1998, V53, P228 HCAPLUS
(31) Schoepp, D; Neuropharmacology 1999, V38, P1431 HCAPLUS
(32) Schulz, B; Neuropharmacology 2001, V41, P1 HCAPLUS
(33) Shigemoto, R; Neurosci Lett 1993, V163, P53 HCAPLUS
(34) Spooren, W; J Pharmacol Exp Ther 2000, V295, P1267 HCAPLUS
(35) Spooren, W; Trends Pharmacol Sci 2001, V22, P331 HCAPLUS

(36) Sumiyoshi, T; Pharmacol Biochem Behav 1994, V47, P553 HCAPLUS
(37) Tatarczynska, E; Br J Pharmacol 2001, V132, P1423 HCAPLUS
(38) Varney, M; J Pharmacol Exp Ther 1999, V290, P170 HCAPLUS
(39) Walker, K; Neuropharmacology 2001, V40, P1 HCAPLUS
(40) Walker, K; Neuropharmacology 2001, V40, P10 HCAPLUS
(41) Wright, R; J Pharmacol Exp Ther 2001, V298, P453 HCAPLUS

IT **528602-22-4**
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(methoxymethyl-MTEP binds to mGluR5 and is a useful tool for studying mGlu5 receptor function/signaling in rodent brain)
RN 528602-22-4 HCAPLUS
CN Pyridine, 3-(methoxymethyl)-5-[(2-methyl-4-thiazolyl)ethynyl]-, labeled with tritium (9CI) (CA INDEX NAME)



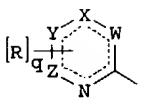
L48 ANSWER 7 OF 7 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:167983 HCAPLUS
DN 134:222706
ED Entered STN: 09 Mar 2001
TI Preparation of heterocyclic compounds as metabotropic glutamate receptor 5 (mGluR5) modulators
IN **Cosford, Nicholas D. P.**; **McDonald, Ian A.**; Bleicher, Leo Solomon; Cube, Rowena V.; Schweiger, Edwin J.; Vernier, Jean-Michel; **Hess, Stephen D.**; **Varney, Mark A.**; Munoz, Benito
PA **Merck** & Co., Inc., USA
SO PCT Int. Appl., 132 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07D277-22
ICS C07D277-24; C07D277-40; C07D213-16; C07D213-30; C07D239-26; C07D263-32; C07D271-06; C07D241-12; C07D249-08; C07D285-00; C07D333-08; C07D417-06; C07D409-06; C07D407-06
CC 28-7 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001016121	A1	20010308	WO 2000-US23923	20000831
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1214303	A1	20020619	EP 2000-957932	20000831
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003508390	T2	20030304	JP 2001-519688	20000831
PRAI	US 1999-387073	A2	19990831		
	US 1999-387135	A2	19990831		
	WO 2000-US23923	W	20000831		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001016121	ICM	C07D277-22
	ICS	C07D277-24; C07D277-40; C07D213-16; C07D213-30; C07D239-26; C07D263-32; C07D271-06; C07D241-12; C07D249-08; C07D285-00; C07D333-08; C07D417-06; C07D409-06; C07D407-06

OS MARPAT 134:222706
GI



I

AB The title compds. I [ALB; A = 5-7 membered ring II (wherein at least one of W, X, Y and Z = (CR)p; p = 0-2, and the remainder of W, X, Y and Z = O, N, S; R = halo, (un)substituted aryl, heterocyclyl, etc.); L = (un)substituted alkenylene, alkynylene, azo; B = (un)substituted alkyl, cycloalkyl, heterocyclyl, etc.] and their pharmaceutically acceptable salts which are capable of modulating the activity of excitatory amino acid receptors such as metabotropic glutamate receptor, were prepared Thus, reacting 2-bromo-1,3-thiazole with phenylacetylene in the presence of CuI, Et3N and PdCl2(PPh3)2 in DME followed by treatment of the resulting 2-(phenylethynyl)-1,3-thiazole with p-TsOH afforded 2-(phenylethynyl)-1,3-thiazole, p-TsOH salt which showed IC50 of 0.1 nM - 10 .mu.M in Ca+2 flux assay and analgesic efficacy in analgesic animal model (CFA model).

ST heterocycle prepn metabotropic glutamate receptor modulator analgesic

IT Glutamate receptors
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(metabotropic, mGluR5; preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

IT Analgesics
(preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

IT 329202-67-7P 329202-70-2P **329202-84-8P 329203-16-9P**
329203-45-4P 329203-62-5P **329204-13-9P 329204-29-7P**
329204-39-9P 329204-47-9P 329204-85-5P 329204-87-7P
329204-97-9P 329205-38-1P 329205-42-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

IT **24622-44-4P 35070-01-0P 111600-92-1P**
129610-15-7P **329202-19-9P** 329202-20-2P **329202-23-5P**
329202-24-6P 329202-25-7P 329202-26-8P **329202-27-9P**
329202-28-0P 329202-29-1P **329202-30-4P** 329202-31-5P
329202-32-6P 329202-33-7P 329202-34-8P 329202-35-9P
329202-36-0P 329202-37-1P 329202-38-2P 329202-40-6P 329202-42-8P
329202-44-0P 329202-46-2P 329202-48-4P 329202-50-8P 329202-52-0P
329202-54-2P 329202-56-4P 329202-58-6P 329202-61-1P 329202-64-4P
329202-73-5P **329202-79-1P 329202-80-4P**
329202-83-7P 329202-87-1P 329202-90-6P 329202-93-9P
329202-98-4P 329203-01-2P 329203-02-3P
329203-05-6P 329203-06-7P 329203-10-3P
329203-13-6P 329203-19-2P 329203-22-7P
329203-25-0P 329203-28-3P 329203-31-8P
329203-36-3P 329203-39-6P 329203-42-1P 329203-48-7P 329203-51-2P
329203-54-5P 329203-57-8P 329203-59-0P 329203-65-8P 329203-78-3P
329203-80-7P **329203-91-0P 329203-94-3P** 329203-98-7P
329204-01-5P **329204-02-6P 329204-07-1P**
329204-10-6P 329204-16-2P 329204-19-5P
329204-22-0P 329204-25-3P 329204-27-5P
329204-31-1P 329204-33-3P 329204-36-6P
329204-41-3P 329204-43-5P 329204-45-7P 329204-49-1P
329204-51-5P 329204-53-7P 329204-55-9P 329204-57-1P 329204-59-3P
329204-62-8P 329204-64-0P 329204-66-2P 329204-72-0P 329204-75-3P
329204-82-2P 329204-89-9P 329204-91-3P **329204-95-7P**
329204-99-1P 329205-01-8P 329205-03-0P
329205-05-2P 329205-07-4P 329205-09-6P
329205-11-0P 329205-13-2P 329205-15-4P
329205-17-6P 329205-19-8P 329205-21-2P 329205-23-4P 329205-28-9P
329205-31-4P 329205-34-7P **329205-40-5P** 329205-44-9P
329205-46-1P 329205-48-3P 329205-50-7P **329205-52-9P**
329205-54-1P 329205-56-3P 329205-58-5P
329205-60-9P 329205-62-1P 329205-64-3P **329205-66-5P**
329205-68-7P 329205-71-2P 329205-74-5P 329205-77-8P
329205-84-7P 329205-86-9P 329205-88-1P
329205-90-5P 329205-92-7P 329205-94-9P 329205-96-1P
329205-98-3P 329206-00-0P 329206-02-2P 329206-04-4P 329206-11-3P
329206-13-5P 329206-16-8P 329206-18-0P 329206-20-4P

329206-22-6P 329206-24-8P 329214-37-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

IT 70-23-5, Ethyl bromopyruvate 78-93-3, 2-Butanone, reactions 78-95-5, Chloroacetone 83-33-0, 1-Indanone 92-66-0, 4-Bromobiphenyl 98-80-6, Phenylboronic acid 100-58-3, Phenylmagnesium bromide 107-19-7, Propargyl alcohol 108-50-9, 2,6-Dimethylpyrazine 108-79-2, 4,6-Dimethyl-2-hydroxypyrimidine 109-01-3, 1-Methylpiperazine 110-89-4, Piperidine, reactions 115-19-5, 2-Methyl-3-butyne-2-ol 118-92-3, Anthranilic acid 120-72-9, Indole, reactions 126-81-8, 5,5-Dimethyl-1,3-cyclohexanedione 141-30-0, 3,6-Dichloropyridazine 352-13-6, 4-Fluorophenylmagnesium bromide 456-48-4, 3-Fluorobenzaldehyde 464-49-3 497-38-1, Norcamphor 502-42-1, Cycloheptanone 502-49-8, Cyclooctanone 529-34-0, .alpha.-Tetralone 530-93-8, .beta.-Tetralone 536-74-3, Phenylacetylene 585-36-4, 3-Trifluoromethylcyclohexanone 589-92-4, 4-Methylcyclohexanone 615-13-4, 2-Indanone 621-79-4, Cinnamamide 622-31-1, syn-Benzaldehyde oxime 623-49-4, Ethyl cyanoformate 624-28-2, 2,5-Dibromopyridine 625-92-3, 3,5-Dibromopyridine 626-55-1, 3-Bromopyridine 627-19-0, 1-Pentyne 627-41-8, Methyl propargyl ether 693-95-8, 4-Methylthiazole 766-49-4, Benzene, 1-ethynyl-2-fluoro- 766-82-5, Benzene, 1-ethynyl-3-methyl 766-98-3, 1-Ethynyl-4-fluorobenzene 917-92-0, 3,3-Dimethyl-1-butyne 931-48-6, Cyclohexylethyne 931-49-7, 1-Ethynylcyclohexene 1066-54-2, Trimethylsilylacetylene 1072-72-6, Tetrahydrothiopyran-4-one 1080-32-6, Diethylbenzyl phosphonate 1193-18-6, 3-Methyl-2-cyclohexen-1-one 1532-97-4, 4-Bromoisoquinoline 1679-18-1, 4-Chlorophenylboronic acid 1692-15-5, Pyridine-4-boronic acid 1692-25-7, Pyridine-3-boronic acid 1757-42-2, 3-Methylcyclopentanone 1945-84-2, 2-Ethynylpyridine 2320-30-1, 3,5-Dimethylcyclohexanone 2816-57-1, 2,6-Dimethylcyclohexanone 3034-48-8, 2-Bromo-5-nitro-1,3-thiazole 3034-53-5, 2-Bromo-1,3-thiazole 3581-91-7, 4,5-Dimethyl-1,3-thiazole 4175-77-3, 2,4-Dibromo-1,3-thiazole 4341-24-6, 5-Methyl-1,3-cyclohexanedione 4360-47-8, Cinnamonitrile 4526-06-1 4595-59-9, 5-Bromopyrimidine 4595-60-2, 2-Bromopyrimidine 4637-24-5 4832-17-1, 2-Decalone 5315-25-3, 2-Bromo-6-methylpyridine 5323-87-5, 3-Ethoxy-2-cyclohexen-1-one 5720-07-0, 4-Methoxyphenylboronic acid 5927-18-4, Trimethylphosphonoacetate 6622-92-0, 2,4-Dimethyl-6-hydroxypyrimidine 6651-36-1 6672-30-6 7214-52-0, cis-3,5-Dimethylcyclohexanone 10472-24-9, Methyl 2-oxocyclopentanecarboxylate 13139-86-1, 4-Anisylmagnesium bromide 13223-25-1, 2-Chloro-4,6-dimethoxypyrimidine 13368-65-5 13472-85-0, 5-Bromo-2-methoxypyridine 13575-75-2, 6,7-Dimethoxy-1-tetralone 14376-79-5, 3,3,5,5-Tetramethylcyclohexanone 14630-40-1, Bis(trimethylsilyl)acetylene 16114-47-9, 3,5-Dimethyl-4-isoxazolylboronic acid 16494-36-3, 2-Iodo-5-methylthiophene 16982-21-1, Ethyl thiooxamate 17356-19-3, 1-Ethynylcyclopentanol 17715-00-3, 3-Cyclohexyl-1-propyne 18871-66-4, N,N-Dimethylacetamide dimethylacetal 19550-72-2, cis-3,4-Dimethylcyclopentanone 20826-04-4, 5-Bromonicotinic acid 23380-78-1 29943-42-8, Tetrahydro-4H-pyran-4-one 32111-21-0, 2-Iodopyrazine 32499-64-2 34259-99-9, 4-Bromo-1,3-thiazole 35590-37-5, 5-Bromonicotinonitrile 38945-21-0, O-Allylhydroxylamine hydrochloride 52482-10-7 54390-97-5, 5-Bromoisothiazole 58372-16-0 69045-79-0, 2-Chloro-5-iodopyridine 74115-12-1, 5-Chloro-3-pyridinol 81166-84-9, Cyclopropyl trimethylsilylacetylene 89878-14-8, Diethyl(3-pyridyl)borane 109299-78-7, (5-Pyrimidinyl)boronic acid 111196-81-7, 2-Chloro-5-ethylpyrimidine 223425-52-3 329206-68-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

IT 694-82-6P 698-16-8P 2510-23-8P 6267-39-6P 6436-59-5P 7210-73-3P 7214-50-8P 13750-63-5P 13750-68-0P 18245-82-4P 20949-84-2P 24202-80-0P 27012-25-5P 29681-44-5P 29947-24-8P 35023-83-7P 40019-47-4P 65832-21-5P 68790-38-5P 74965-38-1P 76632-23-0P 86521-14-4P 86521-15-5P 111600-83-0P 117637-81-7P 123994-49-0P 127053-31-0P 150145-19-0P 154499-80-6P 170859-78-6P 176648-09-2P 179076-90-5P 183608-47-1P 184368-73-8P 193631-86-6P 228405-66-1P 256637-49-7P 291763-66-1P 329202-21-3P 329202-22-4P 329202-76-8P 329203-70-5P 329203-75-0P 329203-85-2P 329203-88-5P 329204-05-9P 329204-69-5P 329204-78-6P 329204-80-0P 329204-93-5P 329205-26-7P 329205-36-9P 329205-79-0P 329205-81-4P 329206-36-2P 329206-38-4P 329206-40-8P 329206-42-0P 329206-45-3P 329206-48-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Agouron Pharma; WO 9603406 A 1996 HCAPLUS
(2) Gasparini; BRITISH JOURNAL OF PHARMACOLOGY 1999, V126(SUPPL PROC), P249
(3) Novartis Erfindungen Verwaltun; WO 9902497 A 1999
(4) Shih; HCAPLUS
(5) Shih; J MED CHEM 1992, V35(6), P1109 HCAPLUS
(6) Varney; HCAPLUS
(7) Varney; BRITISH JOURNAL OF PHARMACOLOGY 1999, V126(SUPPL PROC), P248
(8) Varney; J MED CHEM 1997, V40(16), P2502 HCAPLUS
(9) Varney, M; JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS 1999, V290(1), P170 HCAPLUS

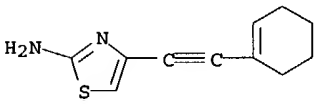
IT **329202-84-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of heterocyclic compds. as metabotropic glutamate receptor 5 (mGluR5) modulators)

RN 329202-84-8 HCAPLUS

CN 2-Thiazolamine, 4-(1-cyclohexen-1-ylethynyl)-, 4-methylbenzenesulfonate (9CI) (CA INDEX NAME)

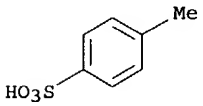
CM 1

CRN 329202-83-7
CMF C11 H12 N2 S



CM 2

CRN 104-15-4
CMF C7 H8 O3 S



=> d all hitstr l51

L51 ANSWER 1 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:672946 HCAPLUS
DN 126:47225
ED Entered STN: 14 Nov 1996
TI Preparation of substituted heterocyclylisoquinolinium salts for the treatment and prevention of neurodegenerative disorders or neurotoxic injuries
IN Dority, John A., Jr.; Earley, William G.; Kumar, Virendra; Mallamo, John P.; Miller, Matthew S.; Subramanyam, Chakrapani
PA Sterling Winthrop Inc., USA
SO U.S., 58 pp., Cont.-in-part of U.S. Ser. No. 121,389, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-54
ICS A61K031-495; A61K031-425; A61K031-415; C07D763-52; C07D415-00; C07D417-02; C07D771-02
NCL 514226800
CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5569655	A	19961029	US 1994-283319	19940729 <--
	EP 647641	A1	19950412	EP 1994-202603	19940910 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	CA 2131967	AA	19950315	CA 1994-2131967	19940913 <--
	AU 9472941	A1	19950330	AU 1994-72941	19940913 <--
	AU 685821	B2	19980129		
	HU 68092	A2	19950529	HU 1994-2629	19940914 <--
	JP 07224065	A2	19950822	JP 1994-219974	19940914 <--
	US 5604224	A	19970218	US 1995-452941	19950530 <--
PRAI	US 1993-121389		19930914 <--		
	US 1994-283319		19940729 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 5569655	ICM	A61K031-54
	ICS	A61K031-495; A61K031-425; A61K031-415; C07D763-52; C07D415-00; C07D417-02; C07D771-02
	NCL	514226800

OS MARPAT 126:47225

GI For diagram(s), see printed CA Issue.

AB The title compds. [I; R1 = H, lower alkyl; R2, R3 = H, lower alkyl; R2R3 = cycloalkyl, lower alkylidene; R4, R5 = lower alkynyl, lower alkoxy, (un)substituted Ph, etc.; R6 = H, lower alkyl, halo, etc.; A = (un)substituted 5- or 6-membered monocyclic aromatic heterocycle (together with C and N atoms to which it is attached); X- = anion; p = 0 when R6 is neg. charged radical; p = 1 when R6 = other than neg. charged radical], useful in the treatment or prevention of neurodegenerative disorders such as Huntington's disease, Alzheimer's disease, amyotrophic lateral sclerosis, Down's Syndrome, senile dementia, multi-infarct dementia and Parkinson's disease, as well as in the treatment or prevention of neurotoxic injuries associated with, e.g., stroke, carbon monoxide poisoning, hyperinsulinemia and cardiac arrest, were prepared Thus, reaction of thiazolo[3,2-b]isoquinolinium perchlorate with 2,2-dimethyl-1,1-diethoxyethylene in MeCN under reflux followed by conversion of the corresponding perchlorate to chloride afforded II which showed IC50 of 173 nM against NMDA-induced neurotoxicity.

ST heterocyclylisoquinolinium prepn neurodegenerative disorder treatment; neurotoxic injury treatment heterocyclylisoquinolinium prepn; NMDA antagonist heterocyclylisoquinolinium prepn; Huntington's disease heterocyclylisoquinolinium prepn; Alzheimer's disease heterocyclylisoquinolinium prepn; amyotrophic lateral sclerosis heterocyclylisoquinolinium prepn; Down's Syndrome heterocyclylisoquinolinium prepn; senile dementia heterocyclylisoquinolinium prepn; multiinfarct dementia heterocyclylisoquinolinium prepn; Parkinson's disease heterocyclylisoquinolinium prepn; stroke heterocyclylisoquinolinium prepn; carbon monoxide poisoning heterocyclylisoquinolinium prepn; hyperinsulinemia heterocyclylisoquinolinium prepn; heart arrest heterocyclylisoquinolinium prepn; ethanothiazoloisoquinolinium prepn NMDA antagonist; nervous system agent heterocyclylisoquinolinium prepn

IT Nervous system
(Huntington's chorea, treatment or prevention; preparation of substituted heterocyclylisoquinolinium salts for the treatment and prevention of neurodegenerative disorders or neurotoxic injuries)

IT **Glutamate antagonists**
(NMDA antagonists; preparation of substituted heterocyclylisoquinolinium salts for the treatment and prevention of neurodegenerative disorders or neurotoxic injuries)

IT Nervous system
(amyotrophic lateral sclerosis, treatment or prevention; preparation of substituted heterocyclylisoquinolinium salts for the treatment and prevention of neurodegenerative disorders or neurotoxic injuries)

IT Heart, disease
(arrest, treatment or prevention; preparation of substituted heterocyclylisoquinolinium salts for the treatment and prevention of neurodegenerative disorders or neurotoxic injuries)

IT Nervous system
(degeneration, treatment or prevention; preparation of substituted heterocyclylisoquinolinium salts for the treatment and prevention of neurodegenerative disorders or neurotoxic injuries)

IT Mental disorder
(dementia, multi-infarct, treatment or prevention; preparation of substituted heterocyclylisoquinolinium salts for the treatment and

prevention of neurodegenerative disorders or neurotoxic injuries)

IT Alzheimer's disease
Nervous system agents
(preparation of substituted heterocyclylisoquinolinium salts for the treatment and prevention of neurodegenerative disorders or neurotoxic injuries)

IT Mental disorder
(senile psychosis, treatment or prevention; preparation of substituted heterocyclylisoquinolinium salts for the treatment and prevention of neurodegenerative disorders or neurotoxic injuries)

IT Brain, disease
(stroke, treatment or prevention; preparation of substituted heterocyclylisoquinolinium salts for the treatment and prevention of neurodegenerative disorders or neurotoxic injuries)

IT Down's syndrome
Parkinson's disease
(treatment or prevention; preparation of substituted heterocyclylisoquinolinium salts for the treatment and prevention of neurodegenerative disorders or neurotoxic injuries)

IT 9004-10-8, Insulin, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(hyperinsulinemia; treatment or prevention; preparation of substituted heterocyclylisoquinolinium salts for the treatment and prevention of neurodegenerative disorders or neurotoxic injuries)

IT 630-08-0, Carbon monoxide, biological studies
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(poisoning; treatment; preparation of substituted heterocyclylisoquinolinium salts for the treatment and prevention of neurodegenerative disorders or neurotoxic injuries)

IT 163628-54-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of substituted heterocyclylisoquinolinium salts for the treatment and prevention of neurodegenerative disorders or neurotoxic injuries)

IT 163628-53-3P 163628-55-5P 163628-56-6P 163628-57-7P 163628-58-8P
163628-59-9P 163628-60-2P 163628-62-4P 163628-63-5P 163628-64-6P
163628-65-7P 163628-66-8P 169376-93-6P 169376-94-7P 169376-95-8P
169376-96-9P 169376-99-2P 169377-00-8P 169377-03-1P 169377-04-2P
169377-06-4P 169377-07-5P 169377-08-6P 169377-12-2P 169377-14-4P
169377-17-7P 169377-18-8P 169377-52-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted heterocyclylisoquinolinium salts for the treatment and prevention of neurodegenerative disorders or neurotoxic injuries)

IT 6384-92-5, NMDA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(preparation of substituted heterocyclylisoquinolinium salts for the treatment and prevention of neurodegenerative disorders or neurotoxic injuries)

IT 78-82-0, Isobutyronitrile 83-33-0, 1-Indanone 86-52-2, 1-Chloromethylnaphthalene 90-96-0 90-98-2 90-99-3, Diphenylmethyl chloride 100-39-0, Benzyl bromide 108-86-1, Bromobenzene, reactions 110-00-9, Furan 110-02-1, Thiophene 119-84-6 122-51-0, Triethyl orthoformate 123-75-1, Pyrrolidine, reactions 271-89-6, Benzofuran 288-13-1, Pyrazole 288-32-4, Imidazole, reactions 288-36-8, 1,2,3-Triazole 288-42-6, Oxazole 288-88-0, 1H-1,2,4-Triazole 345-92-6 488-93-7, Furan-3-carboxylic acid 498-60-2, 3-Furaldehyde 498-62-4, 3-Thiophenecarboxaldehyde 527-72-0, 2-Thienylcarboxylic acid 530-48-3, 1,1-Diphenylethylene 591-51-5, Phenyllithium 611-97-2, Di(p-tolyl)methanone 614-98-2, Ethyl 3-furoate 616-47-7, 1-Methylimidazole 626-05-1, 2,6-Dibromopyridine 626-55-1, 3-Bromopyridine 637-59-2, 3-Phenylpropyl bromide 693-95-8, 4-Methylthiazole 824-94-2, 4-Methoxybenzyl chloride 872-31-1, 3-Bromothiophene 939-26-4, 2-Bromomethylnaphthalene 1868-00-4 1929-29-9, 3-(4-Methoxyphenyl)propionic acid 2398-37-0, 3-Bromoanisole 2743-38-6 3034-53-5, 2-Bromothiazole 3581-89-3, 5-Methylthiazole 4238-71-5, 1-Benzylimidazole 4316-42-1, 1-Butylimidazole 6971-51-3, 3-Methoxybenzylalcohol 7094-34-0 7164-98-9, 1-Phenylimidazole 10111-08-7, 2-Imidazolecarboxaldehyde 10599-70-9, (2,5-Dimethyl-3-acetyl)furan 13414-95-4 16806-93-2, 4,5,6,7-Tetrahydrobenzofuran-4-one

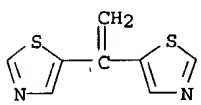
18982-54-2, 2-Bromobenzylalcohol 19524-06-2, 4-Bromopyridine hydrochloride 22037-28-1, 3-Bromofuran 25032-74-0 39193-85-6 39687-95-1, Methyl isocyanoacetate 79265-30-8, 2-Trimethylsilylthiazole 87630-35-1, 1-Triisopropylsilylpyrrole 108153-93-1, 4,5,6,7-Tetrahydrobenzofuran-7-one 167075-59-4 170487-35-1, 4,5,6,7-Tetrahydro-3-methylbenzisoxazol-7-one
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of substituted heterocyclylisoquinolinium salts for the treatment and prevention of neurodegenerative disorders or neurotoxic injuries)

IT 704-38-1P 1120-87-2P, 4-Bromopyridine 1488-34-2P 1961-97-3P, 3-Phenylindene 2642-81-1P 2919-20-2P 4356-69-8P 6002-15-9P, 1-Phenyl-2-imidazolecarboxaldehyde 6086-21-1P 6175-14-0P 6918-15-6P 10045-65-5P, 1-Benzyl-2-imidazolecarboxaldehyde 10200-59-6P, 2-Thiazolecarboxaldehyde 10605-43-3P 10605-50-2P 13336-31-7P, 4-Methoxy-1-indanone 13623-25-1P, 6-Methoxy-1-indanone 13750-68-0P, 4-Methyl-2-thiazolecarboxaldehyde 13750-81-7P 13750-82-8P 13838-78-3P, 5-Methyl-2-thiazolecarboxaldehyde 17920-86-4P 20583-35-1P 24295-04-3P 25603-17-2P 26453-81-6P 29265-85-8P 30078-67-2P 30782-41-3P 31794-11-3P 31936-92-2P 35779-35-2P 39240-84-1P 40731-98-4P, 4-Hydroxy-1-indanone 42772-87-2P 52070-18-5P 55707-55-6P 56643-92-6P 56643-95-9P, 1-(4-Methoxybenzyl)imidazole 57803-92-6P 72459-37-1P 77605-69-7P, 5-Methoxy-3-phenylindene 87630-36-2P 91272-98-9P 95460-12-1P, 1-(4-Methoxybenzyl)imidazole-2-carboxaldehyde 98318-77-5P 98946-66-8P 99651-37-3P 104053-68-1P, 6-Methoxy-1-phenyl-1-indanol 105399-18-6P 118994-84-6P, 4-Oxazolecarboxaldehyde 127158-63-8P 130551-90-5P 148900-66-7P 155855-38-2P 156841-32-6P 161227-55-0P 161227-56-1P 161227-57-2P 161227-84-5P 161227-85-6P 161227-86-7P **161227-87-8P** 161227-88-9P 163190-80-5P 163190-81-6P 163190-95-2P 163191-01-3P 163628-41-9P 163628-43-1P 163628-45-3P 163628-48-6P 163628-50-0P 163628-51-1P 166885-99-0P 167075-62-9P 169377-19-9P 169377-20-2P 169377-21-3P 169377-22-4P 169377-25-7P 169377-26-8P 169377-27-9P 169377-28-0P 169377-29-1P 169377-33-7P 169377-34-8P 169377-36-0P 169377-39-3P 169377-40-6P 169377-41-7P 169377-43-9P 169377-49-5P 169377-51-9P 169377-55-3P 169377-57-5P 169377-58-6P 169377-60-0P 169377-62-2P 169377-64-4P 169377-66-6P 169377-67-7P 169377-68-8P 169377-70-2P 169377-72-4P 169377-73-5P 169377-77-9P 169377-79-1P 169377-81-5P 169377-82-6P 169377-83-7P 169377-85-9P 169377-87-1P 169377-88-2P 169377-90-6P 169377-93-9P 169377-96-2P 169377-98-4P 169378-00-1P 169378-04-5P 169378-05-6P 169378-06-7P 169378-10-3P 169378-11-4P 169378-12-5P 169378-16-9P 169378-17-0P 169378-18-1P 169378-22-7P 169378-24-9P 169378-25-0P 169378-28-3P 169378-29-4P 169378-30-7P 169378-31-8P 169378-33-0P 169378-35-2P 169378-37-4P 169378-39-6P, 4-Methoxy-1-phenyl-1-indanol 169378-45-4P 169378-46-5P 169378-49-8P 169378-51-2P 169378-52-3P, 1-Butyl-2-imidazolecarboxaldehyde 169378-53-4P 170486-33-6P 170486-34-7P 170486-48-3P 170486-49-4P 170486-55-2P 170486-58-5P 170486-59-6P 170486-63-2P 170487-38-4P, Methyl 4-oxazolecarboxylate 182802-19-3P, 7-Methoxy-3-phenylindene 182802-20-6P 182802-34-2P 184538-02-1P 184538-04-3P 184538-06-5P 184583-77-5P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted heterocyclylisoquinolinium salts for the treatment and prevention of neurodegenerative disorders or neurotoxic injuries)

IT 182802-18-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of substituted heterocyclylisoquinolinium salts for the treatment and prevention of neurodegenerative disorders or neurotoxic injuries)

IT **161227-87-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of substituted heterocyclylisoquinolinium salts for the treatment and prevention of neurodegenerative disorders or neurotoxic injuries)

RN 161227-87-8 HCAPLUS
CN Thiazole, 5,5'-ethenylidenebis- (9CI) (CA INDEX NAME)



=> d all hitstr l51 2

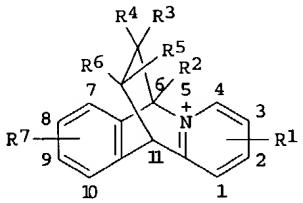
L51 ANSWER 2 OF 2 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:580564 HCAPLUS
DN 125:328525
ED Entered STN: 30 Sep 1996
TI Substituted 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA antagonists useful for the treatment of neurodegenerative disorders or neurotoxic injuries
IN Dehaven-Hudkins, Diane L.; Dority, John A., Jr.; Earley, William G.; Kumar, Virendra; Mallamo, John P.; Miller, Matthew S.; Subramanyam, Chakrapani
PA Sterling Winthrop Inc., USA
SO U.S., 80 pp., Cont.-in-part of U.S. Ser. No. 121,127, abandoned.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-44
ICS C07D471-00
NCL 514278000
CC 27-18 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 63
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5554620	A	19960910	US 1994-283317	19940729 <--
	EP 656359	A1	19950607	EP 1994-202601	19940910 <--
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	CA 2131966	AA	19950315	CA 1994-2131966	19940913 <--
	AU 9472940	A1	19950330	AU 1994-72940	19940913 <--
	AU 683679	B2	19971120		
	HU 68530	A2	19950628	HU 1994-2634	19940914 <--
	JP 07179462	A2	19950718	JP 1994-220255	19940914 <--
	US 5631264	A	19970520	US 1995-449125	19950524 <--
PRAI	US 1993-121127		19930914 <--		
	US 1994-283317		19940729 <--		

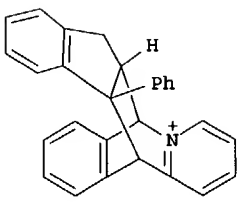
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 5554620	ICM	A61K031-44
	ICS	C07D471-00
	NCL	514278000

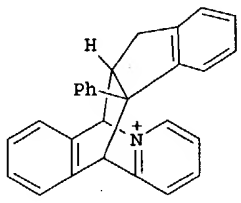
OS MARPAT 125:328525
GI



I



II



III

AB Substituted 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts I.(X-)p are claimed, wherein: R1 is hydrogen, or from one to four, the same or different, substituents in any of the 1, 2, 3, or 4 positions selected

from the group consisting of, e.g.; lower alkoxy, lower alkyl, halogen, hydroxy; R2 is hydrogen, lower alkyl, cyano or lower-alkoxycarbonyl; R3 and R4 are independently hydrogen, or lower alkyl; or R3 and R4 together form a cycloalkyl ring, or a lower alkylidene group; R5 and R6 are independently hydrogen, Ph, furyl or benzofuryl; or R3 and R5, and/or R4 and R6 taken together with the carbon atoms to which they are attached form a bicyclic ring system; R7 is hydrogen, or from one to four, the same or different, substituents in any of the 7, 8, 9, or 10 positions selected from the group consisting of, e.g., lower alkyl, lower alkanoyloxy, halogen, nitro, hydroxy, lower alkoxy, methylenedioxy; X- is an anion; and, p is zero when R7 is a neg. charged radical and p is one when R7 is other than a neg. charged radical (with provisos); or pharmaceutical compns. containing them for the treatment of neurodegenerative disorders or neurotoxic injuries. Thus, e.g., treatment of 1-indanone with PhLi followed by acid afforded 3-phenyl-1H-indene; 2-pyridinecarboxaldehyde was converted to its ethylene acetal [2-(1,3-dioxolan-2-yl)pyridine], and the latter alkylated with benzyl bromide to afford 2-(1,3-dioxolan-2-yl)-1-benzylpyridinium bromide; cyclization of the latter followed by anion exchange afforded benzo[b]quinolizinium hexafluorophosphate; finally, cycloaddn. reaction of the latter with 3-phenyl-1H-indene afforded an isomeric mixture of 6,11[[2',3']-3'-phenylindanyl]6,11-dihydrobenzo[b]quinolizinium hexafluorophosphate (II/III.PF6-) which exhibited binding to the PCP receptor with Ki = 7.58 nM. Data were also presented for antagonism by I of NMDA-induced neurotoxicity in cultured neurons as well as for the protection effect of I in a rat ischemia model.

ST ethanodihydrobenzoquinolizinium salt neurodegenerative disorder neurotoxic injury; benzoquinolizinium ethanodihydro neurodegenerative disorder neurotoxic injury; NMDA antagonist ethanodihydrobenzoquinolizinium salt

IT Nervous system
(disease, degeneration, substituted 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA antagonists useful for the treatment of neurodegenerative disorders or neurotoxic injuries)

IT **Neurotransmitter antagonists**
(**methyl-D-aspartate**, substituted 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA antagonists useful for the treatment of neurodegenerative disorders or neurotoxic injuries)

IT Brain, disease
(stroke, treatment; substituted 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA antagonists useful for the treatment of neurodegenerative disorders or neurotoxic injuries)

IT 183183-48-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(geometric isomer mixture; substituted 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA antagonists useful for the treatment of neurodegenerative disorders or neurotoxic injuries)

IT 169377-40-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(in situ allene precursor; substituted 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA antagonists useful for the treatment of neurodegenerative disorders or neurotoxic injuries)

IT 170484-29-4P 170484-30-7P 170484-44-3P 170484-50-1P 170484-51-2P
170484-58-9P 170484-93-2P 170485-29-7P 170714-30-4P 170714-31-5P
170714-42-8P 170714-49-5P 170714-55-3P 170714-70-2P 170714-71-3P
170897-48-0P 182802-51-3P 182802-52-4P 182802-65-9P 182802-66-0P
182802-68-2P 182802-69-3P 182967-74-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(substituted 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA antagonists useful for the treatment of neurodegenerative disorders or neurotoxic injuries)

IT 161227-63-0P 170484-81-8P 170485-37-7P 170485-69-5P 170485-95-7P
170486-26-7P 170486-61-0P 170487-16-8P 170714-64-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(substituted 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA antagonists useful for the treatment of neurodegenerative disorders or neurotoxic injuries)

IT 161227-46-9P 161227-47-0P 161227-48-1P 161227-51-6P 161227-53-8P

161227-54-9P 161227-68-5P 161227-69-6P 161227-70-9P 161227-71-0P
161227-72-1P 161227-73-2P 161227-74-3P 161227-76-5P 161227-78-7P
161227-80-1P 161227-81-2P 161227-82-3P 161227-83-4P 161227-90-3P
170484-13-6P 170484-15-8P 170484-17-0P 170484-19-2P 170484-21-6P
170484-25-0P 170484-27-2P 170484-32-9P 170484-34-1P 170484-39-6P
170484-41-0P 170484-42-1P 170484-46-5P 170484-47-6P 170484-53-4P
170484-54-5P 170484-56-7P 170484-60-3P 170484-61-4P 170484-63-6P
170484-64-7P 170484-66-9P 170484-67-0P 170484-69-2P 170484-76-1P
170484-77-2P 170484-78-3P 170484-79-4P 170484-83-0P 170484-85-2P
170484-86-3P 170484-88-5P 170484-89-6P 170484-94-3P 170484-95-4P
170484-97-6P 170484-98-7P 170485-00-4P 170485-01-5P 170485-03-7P
170485-05-9P 170485-07-1P 170485-08-2P 170485-10-6P 170485-11-7P
170485-13-9P 170485-15-1P 170485-17-3P 170485-19-5P 170485-20-8P
170485-22-0P 170485-24-2P 170485-26-4P 170485-27-5P 170485-31-1P
170485-32-2P 170485-34-4P 170485-35-5P 170485-38-8P 170485-40-2P
170485-41-3P 170485-43-5P 170485-45-7P 170485-46-8P 170485-48-0P
170485-49-1P 170485-51-5P 170485-52-6P 170485-54-8P 170485-56-0P
170485-58-2P 170485-61-7P 170485-62-8P 170485-63-9P 170485-64-0P
170485-70-8P 170485-71-9P 170485-72-0P 170485-73-1P 170485-75-3P
170485-77-5P 170485-78-6P 170485-79-7P 170485-81-1P 170485-82-2P
170485-84-4P 170485-85-5P 170485-86-6P 170485-88-8P 170485-89-9P
170485-91-3P 170485-93-5P 170485-94-6P 170485-97-9P 170485-99-1P
170486-00-7P 170486-02-9P 170486-03-0P 170486-04-1P 170486-06-3P
170486-08-5P 170486-09-6P 170486-11-0P 170486-12-1P 170486-14-3P
170486-15-4P 170486-16-5P 170486-18-7P 170486-19-8P 170486-21-2P
170486-23-4P 170486-24-5P 170486-27-8P 170486-29-0P 170486-31-4P
170486-95-0P 170714-32-6P 170714-33-7P 170714-35-9P 170714-37-1P
170714-39-3P 170714-41-7P 170714-45-1P 170714-47-3P 170714-51-9P
170714-53-1P 170714-57-5P 170714-61-1P 170714-63-3P 170714-66-6P
170714-68-8P 170714-73-5P 182802-22-8P 182802-50-2P 182802-56-8P
182802-57-9P 182802-59-1P 182802-60-4P 182802-63-7P 182802-73-9P
182802-75-1P 182803-14-1P 182803-16-3P 182803-17-4P 182803-19-6P
182967-75-5P 182967-76-6P 182967-77-7P 182967-79-9P 183071-67-2P
183071-68-3P 183183-46-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(substituted 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA antagonists useful for the treatment of neurodegenerative disorders or neurotoxic injuries)

IT 170486-54-1P 182802-18-2P, 1-Acetoxy-1-phenylindan
RL: BYP (Byproduct); PREP (Preparation)
(substituted 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA antagonists useful for the treatment of neurodegenerative disorders or neurotoxic injuries)

IT 75-26-3, Isopropyl bromide 78-95-5, Chloroacetone 79-31-2, Isobutyric acid 83-33-0, 1-Indanone 90-96-0, Bis(p-methoxyphenyl) ketone 90-98-2, Bis(p-chlorophenyl) ketone 95-13-6, Indene 100-11-8, 4-Nitrobenzyl bromide 100-39-0, Benzyl bromide 100-83-4 104-83-6, p-Chlorobenzyl chloride 107-19-7, Propargyl alcohol 108-86-1, reactions 109-72-8, n-Butyllithium, reactions 110-00-9, Furan 110-02-1, Thiophene 111-64-8, Octanoyl chloride 111-83-1, Octyl bromide 112-80-1, 9-Octadecenoic acid (Z)-, reactions 119-61-9, Benzophenone, reactions 119-84-6 127-66-2 271-89-6, Benzofuran 288-36-8, 1,2,3-Triazole 288-42-6, Oxazole 288-88-0, 1H-1,2,4-Triazole 329-15-7, p-Trifluoromethylbenzoyl chloride 345-92-6, Bis(4-fluorophenyl) ketone 372-47-4, 3-Fluoropyridine 459-46-1, 4-Fluorobenzyl bromide 486-25-9, 9-Fluorenone 488-93-7, Furan-3-carboxylic acid 495-76-1, 3,4-Methylenedioxybenzyl alcohol 498-60-2, 3-Furaldehyde 498-62-4, 3-Thiophenecarboxaldehyde 527-72-0, 2-Thienylcarboxylic acid 530-48-3, 1,1-Diphenylethene 586-37-8 589-15-1, p-Bromobenzyl bromide 591-51-5, Phenyllithium 598-21-0, Bromoacetyl bromide 611-97-2, Di-p-tolyl ketone 614-98-2, Ethyl 3-furoate 615-59-8, 2,5-Dibromotoluene 615-74-7, 4-Chloro-3-Hydroxytoluene 626-05-1 626-55-1, 3-Bromopyridine 778-66-5, 1,1-Diphenylprop-1-ene 824-94-2, p-Methoxybenzyl chloride 824-98-6, 3-Methoxybenzyl chloride 872-31-1, 3-Bromothiophene 1003-67-4, 4-Picoline N-oxide 1121-60-4, 2-Pyridinecarboxaldehyde 1122-72-1, 6-Methyl-2-pyridinecarboxaldehyde 1868-00-4, 3,3'-Bis(trifluoromethyl)benzophenone 1929-29-9, 3-(4-Methoxyphenyl)propionic acid 2398-37-0, 3-Bromoanisole 2743-38-6, Dibenzoyl-L-tartaric acid 3034-53-5, 2-Bromothiazole 3042-81-7, Methyl bromophenylacetate 3282-30-2, Trimethylacetyl chloride 3990-03-2, Maleic acid monoethyl ester 5361-46-6 6126-10-9, 1-(p-Toluenesulfonyl)pyrazole 6630-33-7, 2-Bromobenzaldehyde 6971-51-3, 3-Methoxybenzyl alcohol 7035-02-1, o-Methoxybenzyl chloride 7094-34-0, 3,3'-Dichlorobenzophenone

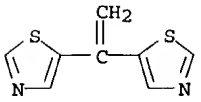
7295-76-3, 3-Methoxypyridine 10599-70-9, 3-Acetyl-2,5-dimethylfuran
13170-43-9, Trimethylsilylmethylmagnesium chloride 13414-95-4,
4,5,6,7-Tetrahydrothianaphthen-4-one 14114-05-7,
Cyclopropyltriphenylphosphonium bromide 14794-31-1 16806-93-2,
4,5,6,7-Tetrahydrobenzofuran-4-one 17026-42-5, Dibenzoyl-D-tartaric acid
17347-61-4, 3,3-Dimethylsuccinic anhydride 18507-95-4,
Benzo[b]quinolizinium perchlorate 18595-18-1, Methyl
3-amino-4-methylbenzoate 18982-54-2, o-Bromobenzyl alcohol 19524-06-2,
4-Bromopyridine hydrochloride 22037-28-1, 3-Bromofuran 25032-74-0,
3,3'-Dibromobenzophenone 27104-73-0, Methyl 3-isoquinolinecarboxylate
33524-31-1, 2,5-Dimethoxybenzyl alcohol 39193-85-6, 3,3'-
Dimethoxybenzophenone 39687-95-1, Methyl isocyanoacetate 54416-76-1,
1,1-Di-2-pyridylethene 56643-95-9 62456-33-1 67088-76-0,
Di(pyrazol-4-yl) ketone 73942-52-6 76513-69-4, 2-
(Trimethylsilylethoxy)methyl chloride 79265-30-8, 2-
Trimethylsilylthiazole 87630-35-1, 1-(Triisopropylsilyl)pyrrole
91272-98-9, 1-(1-Pyrrolidinomethyl)pyrazole 97407-07-3 108153-93-1,
4,5,6,7-Tetrahydrobenzofuran-7-one 131674-46-9, Bis(2-chloropyridin-3-
yl)methanol 133560-57-3 141776-91-2, 3,5-Difluorobenzyl bromide
145162-51-2, 1-(p-Methoxybenzyl)pyrazole 168886-63-3,
10-Hydroxybenzo[b]quinolizinium bromide 168886-97-3,
o-Bromo-m-methylbenzyl alcohol 170487-35-1, 4,5,6,7-Tetrahydro-3-
methylbenzisoxazol-7-one 173730-28-4 182803-24-3, 9-
Chlorobenzo[b]quinolizinium bromide
RL: RCT (Reactant); RACT (Reactant or reagent)
(substituted 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as
NMDA antagonists useful for the treatment of neurodegenerative
disorders or neurotoxic injuries)

IT 349-95-1P, p-Trifluoromethylbenzyl alcohol 402-49-3P,
p-Trifluoromethylbenzyl bromide 704-38-1P, Di-2-thienyl ketone
1120-87-2P, 4-Bromopyridine 1488-34-2P, 1,1-Bis(3-methoxyphenyl)ethylene
1695-36-9P, 9-Fluorobenzo[b]quinolizinium perchlorate 1695-37-0P,
9-Chlorobenzo[b]quinolizinium perchlorate 1695-38-1P,
9-Bromobenzo[b]quinolizinium bromide 1849-53-2P, 3-Methoxypyridine-2-
carboxaldehyde 1961-97-3P, 3-Phenylindene 2642-81-1P,
1,1-Bis(p-chlorophenyl)ethylene 2919-20-2P, 1,1-Di-p-tolylethene
4356-69-8P, 1,1-Bis(p-methoxyphenyl)ethylene 4425-82-5P,
9-Methylenefluorene 4494-18-2P, 1-Isoquinolinecarboxaldehyde
5470-80-4P, 3-Isoquinolinecarboxaldehyde 5693-54-9P,
2-(1,3-Dioxolan-2-yl)pyridine 6175-14-0P, 1,1-Bis(4-fluorophenyl)ethene
6918-15-6P, Di-4-pyridyl ketone 7547-88-8P, Benzo[b]quinolizinium
bromide 7547-93-5P, 6-Methylbenzo[b]quinolizinium perchlorate
7632-57-7P, (Diphenylmethylene)cyclopropane 10605-43-3P,
1,1-Bis(4-bromophenyl)ethylene 10605-50-2P, 1,1-Bis(m-
chlorophenyl)ethylene 13336-31-7P, 4-Methoxyindan-1-one 13623-25-1P,
6-Methoxy-1-indanone 13726-17-5P, 4-Chloro-3-methoxybenzyl alcohol
14313-09-8P 17920-86-4P, Di-2-furyl ketone 20583-35-1P, Di-5-pyrazolyl
ketone 23308-82-9P 26066-15-9P, m-Isopropoxybenzyl alcohol
26453-81-6P, Di-3-thienyl ketone 27104-72-9P, Methyl
1-isoquinolinecarboxylate 27755-38-0P, 9-Nitrobenzo[b]quinolizinium
perchlorate 29265-85-8P, 1,1-Bis(3-bromophenyl)ethylene 30782-41-3P,
1,1-Di-2-thienylethylene 31224-43-8P, 3-Fluoro-2-pyridinecarboxaldehyde
31794-11-3P, 1-(p-Methoxybenzyl)-1,2,3-triazole 31936-92-2P,
Di-3-thienylmethanol 34160-40-2P, 6-Bromo-2-pyridinecarboxaldehyde
35779-35-2P, Di-3-pyridyl ketone 36680-28-1P 38674-98-5P, Octyl
bromoacetate 40731-98-4P, 4-Hydroxyindan-1-one 42772-87-2P
50585-79-0P, 10-Nitrobenzo[b]quinolizinium perchlorate 53547-60-7P,
4-Methylpyridine-2-carboxaldehyde 54356-08-0P 55707-55-6P,
Di-2-thiazolyl ketone 57803-92-6P, 3-(3-Methoxyphenyl)indene
71255-11-3P, Bis(2-methoxypyridin-3-yl) ketone 71721-60-3P
73909-16-7P, 4-Chloro-3-methoxytoluene 74808-20-1P, 4-
Methylbenzo[b]quinolizinium perchlorate 75792-33-5P,
3-Isopropoxybenzaldehyde 77605-69-7P, 5-Methoxy-3-phenylindene
81430-18-4P, 3-Ethoxycarbonyl-3,3-dimethylpropionyl chloride
85740-98-3P, 4-Chloro-3-methoxybenzoic acid 87630-36-2P,
3-Bromo-1-triisopropylsilylpyrrole 97360-71-9P, 1-Benzyl-2-(1,3-Dioxolan-
2-yl)pyridinium bromide 98946-66-8P, 1,1-Di-3-thienylethylene
104053-68-1P, 6-Methoxy-1-phenyl-indan-1-ol 105399-18-6P,
1,1-Di(2-furyl)ethylene 107541-66-2P 111588-45-5P 112625-92-0P,
6-Cyanobenzo[b]quinolizinium perchlorate 115201-42-8P,
1-(p-Methoxybenzyl)-1,2,4-triazole 118994-84-6P, 4-Oxazolecarboxaldehyde
121925-55-1P, 3-Ethoxycarbonyl-3,3-dimethylpropionic acid 127158-63-8P,
Di-3-furyl ketone 130551-90-5P, 1,1-Di(4-oxazolyl)methanol
131674-48-1P, Bis(2-chloropyridin-3-yl) ketone 136105-40-3P,
2,5-Dibromobenzyl bromide 148900-66-7P, 3-(N-Methyl-N-
methoxycarbamoyl)furan 155855-38-2P, 1,1-Bis(m-

trifluoromethylphenyl)ethylene 156600-09-8P, Benzo[b]quinolizinium hexafluorophosphate 156841-32-6P, 1-(3-Methoxyphenyl)indan-1-ol 161227-55-0P 161227-56-1P 161227-57-2P 161227-60-7P 161227-61-8P 161227-64-1P 161227-65-2P 161227-84-5P, 1,1-Di-3-pyridylethene 161227-85-6P, 1,1-Di-4-pyridylethylene 161227-86-7P, 1,1-Di-3-furylethene **161227-87-8P**, 1,1-Di(5-thiazolyl)ethylene 161227-88-9P, 1,1-Di(4-oxazolyl)ethylene 162468-75-9P 163190-83-8P, 10-Methoxy-6-methylbenzo[b]quinolizinium perchlorate 163190-85-0P, 10-Methoxybenzo[b]quinolizinium perchlorate 163190-87-2P 163190-91-8P, 9,10-Methylenedioxybenzo[b]quinolizinium perchlorate 163190-93-0P 163190-99-6P, 6-Butylbenzo[b]quinolizinium perchlorate 166886-01-7P, 10-Hydroxybenzo[b]quinolizinium perchlorate 166886-03-9P, 10-Acetoxybenzo[b]quinolizinium perchlorate 167075-59-4P 167075-62-9P 167165-98-2P, 9-Chloro-10-hydroxybenzo[b]quinolizinium perchlorate 167166-00-9P, 4-Chlorobenzo[b]quinolizinium perchlorate 167166-38-3P 168886-66-6P, 7-Methoxybenzo[b]quinolizinium hexafluorophosphate 168886-67-7P 168886-69-9P, 9-Methoxybenzo[b]quinolizinium hexafluorophosphate 168886-75-7P, 9-(Trifluoromethyl)benzo[b]quinolizinium hexafluorophosphate 168886-79-1P, 8,10-Difluorobenzo[b]quinolizinium hexafluorophosphate 168886-81-5P, 9-Chlorobenzo[b]quinolizinium chloride 168886-82-6P 168886-83-7P 168886-87-1P 168886-89-3P, 1-Methoxybenzo[b]quinolizinium perchlorate 168886-90-6P 168886-92-8P 168886-98-4P 168887-00-1P, 10-Methylbenzo[b]quinolizinium perchlorate 168887-02-3P, 7,10-Dimethoxybenzo[b]quinolizinium perchlorate 168887-04-5P, 8-Methoxybenzo[b]quinolizinium hexafluorophosphate 168887-08-9P, 2-Methylbenzo[b]quinolizinium perchlorate 169377-19-9P 169377-20-2P 169377-21-3P 169377-22-4P 169377-25-7P 169377-26-8P 169377-27-9P 169377-28-0P 169377-29-1P 169377-33-7P 169377-34-8P, Bis(6-methoxypyridin-2-yl) ketone 169377-36-0P 169377-39-3P 169377-93-9P 169378-39-6P, 4-Methoxy-1-phenyl-indan-1-ol 169378-45-4P, 4-Ethoxy-6,7-dihydrobenzofuran 169378-46-5P 169378-49-8P, Di(5-thiazolyl) ketone 170486-33-6P, 1-(3-Furyl)indan-1-ol 170486-34-7P 170486-38-1P 170486-39-2P 170486-40-5P, 9-Hydroxybenzo[b]quinolizinium bromide 170486-41-6P 170486-43-8P 170486-48-3P 170486-49-4P, Di-4-oxazolyl ketone 170486-50-7P 170486-53-0P, 7,10-Dibromobenzo[b]quinolizinium perchlorate 170486-55-2P 170486-57-4P 170486-59-6P, 1,1-Bis(6-methoxypyridin-2-yl)ethylene 170486-63-2P 170486-65-4P 170486-67-6P 170486-70-1P 170486-71-2P 170486-72-3P 170486-73-4P 170486-74-5P 170486-75-6P 170486-76-7P 170486-78-9P 170486-79-0P, 1,1-Bis(2-methoxypyridin-3-yl)ethylene 170486-80-3P 170486-81-4P 170486-83-6P 170486-84-7P 170486-85-8P 170486-87-0P, 1-Hydroxybenzo[b]quinolizinium perchlorate 170486-88-1P 170486-90-5P 170486-93-8P, 6-(Methoxycarbonyl)benzo[b]quinolizinium perchlorate 170486-97-2P 170486-98-3P 170486-99-4P 170487-00-0P 170487-01-1P 170487-02-2P, 10-(Chloromethyl)benzo[b]quinolizinium perchlorate 170487-04-4P 170487-05-5P 170487-06-6P 170487-07-7P 170487-08-8P 170487-09-9P 170487-10-2P 170487-12-4P 170487-17-9P 170487-19-1P 170487-21-5P 170487-22-6P 170487-23-7P 170487-24-8P, 3-Hydroxybenzo[b]quinolizinium perchlorate 170487-25-9P 170487-29-3P 170487-30-6P 170487-32-8P, 1-Fluorobenzo[b]quinolizinium perchlorate 170487-34-0P 170487-38-4P, Methyl 4-oxazolecarboxylate 170487-39-5P, 2-Cyano-4-methylpyridine N-oxide 170487-40-8P, Methyl indazole-6-carboxylate 182802-19-3P, 7-Methoxy-3-phenylindene 182802-20-6P, 3-(3-Furyl)indene 182802-34-2P 182802-54-6P 182802-62-6P 182802-70-6P 182802-74-0P 182802-83-1P 182802-89-7P 182802-90-0P 182802-91-1P 182802-95-5P 182802-97-7P 182802-98-8P 182803-01-6P 182803-05-0P 182803-08-3P 182803-09-4P 182803-10-7P 182803-11-8P 182803-20-9P 182803-21-0P, 9,10-Methylenedioxybenzo[b]quinolizinium hexafluorophosphate 182803-23-2P 182803-25-4P 182803-26-5P 182803-27-6P 182967-86-8P 182967-87-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(substituted 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA antagonists useful for the treatment of neurodegenerative disorders or neurotoxic injuries)

IT **161227-87-8P**, 1,1-Di(5-thiazolyl)ethylene
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(substituted 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA antagonists useful for the treatment of neurodegenerative disorders or neurotoxic injuries)

RN 161227-87-8 HCAPLUS
CN Thiazole, 5,5'-ethenylidenebis- (9CI) (CA INDEX NAME)



=> d all hitstr 152 tot

L52 ANSWER 1 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2002:717057 HCAPLUS
DN 137:226598
ED Entered STN: 20 Sep 2002
TI Dna-cleaving antitumor agents
IN Kerwin, Sean Michael; David, Wendi M.
PA Research Development Foundation, USA
SO U.S. Pat. Appl. Publ., 59 pp., Cont.-in-part of U. S. 6,297,284.
CODEN: USXXCO
DT Patent
LA English
IC ICM C07C247-00
ICS A61K031-695; A61K031-655
NCL 514151000
CC 1-6 (Pharmacology)
Section cross-reference(s): 27, 28
FAN.CNT 4

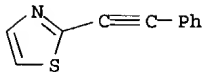
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002132797	A1	20020919	US 2001-967133	20010928 <--
	US 6686345	B2	20040203		
	US 6297284	B1	20011002	US 2000-533723	20000323 <--
PRAI	US 1998-93112P	P	19980716 <--		
	US 1999-356303	A2	19990716 <--		
	US 2000-533723	A2	20000323		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 2002132797	ICM	C07C247-00
	ICS	A61K031-695; A61K031-655
	NCL	514151000

OS MARPAT 137:226598
AB A chemical composition and method of use of the composition is described. The chemical composition includes an aza-enediyne, aza-enyne allene, or an aza-diallene. These compound are preferably non-hydrolyzable, cationic compds. that bind to nucleic acids. In addition it is believed that these compds. may undergo chemical reactions in the presence of a nucleic acid to generate reactive intermediates that cleave nucleic acids.
ST azaenediyne prepn DNA cleaving antitumor agent; azadiallene prepn DNA cleaving antitumor agent; azaenyne allene prepn DNA cleaving antitumor agent
IT Intercalation
(agents, nucleic acid-interactive; aza-enediynes and aza-enyne allenes and aza-diallenes as DNA-cleaving antitumor agents)
IT Glycosides
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(amino, nucleic acid-interactive; aza-enediynes and aza-enyne allenes and aza-diallenes as DNA-cleaving antitumor agents)
IT Peptides, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(and peptoids, nucleic acid-interactive; aza-enediynes and aza-enyne allenes and aza-diallenes as DNA-cleaving antitumor agents)
IT Alkylating agents, biological
Antitumor agents
Drug delivery systems
Human
Metalation
(aza-enediynes and aza-enyne allenes and aza-diallenes as DNA-cleaving antitumor agents)
IT Biradicals
DNA
Nucleic acids
RNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(aza-enediynes and aza-enyne allenes and aza-diallenes as DNA-cleaving

antitumor agents)
IT DNA
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(cleavage; aza-enediynes and aza-enyne allenes and aza-diallenes as DNA-cleaving antitumor agents)
IT Onium compounds
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(iminium; aza-enediynes and aza-enyne allenes and aza-diallenes as DNA-cleaving antitumor agents)
IT Carbohydrates, biological studies
Crown ethers
Oligonucleotides
Oligosaccharides, biological studies
Peptide nucleic acids
Porphyrins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(nucleic acid-interactive; aza-enediynes and aza-enyne allenes and aza-diallenes as DNA-cleaving antitumor agents)
IT Neoplasm
(treatment; aza-enediynes and aza-enyne allenes and aza-diallenes as DNA-cleaving antitumor agents)
IT **35070-01-0P** 37536-65-5P 325793-43-9P
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(aza-enediynes and aza-enyne allenes and aza-diallenes as DNA-cleaving antitumor agents)
IT 255716-41-7P 321200-65-1P 363134-45-6P 363134-46-7P 363134-47-8P
363134-48-9P 363134-49-0P 363134-51-4P 363134-53-6P 459832-26-9P
459832-28-1P 459832-30-5P 459832-32-7P 459832-34-9P 459832-36-1P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aza-enediynes and aza-enyne allenes and aza-diallenes as DNA-cleaving antitumor agents)
IT 362604-39-5 363134-56-9 363134-57-0
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aza-enediynes and aza-enyne allenes and aza-diallenes as DNA-cleaving antitumor agents)
IT 86-81-7, 3,4,5-Trimethoxybenzaldehyde 95-54-5, 1,2-Benzenediamine, reactions 100-39-0 109-04-6 136-95-8, 2-Benzothiazolamine 333-27-7
536-74-3 583-39-1 668-94-0 766-97-2 1066-54-2 2579-22-8
3034-53-5 4595-60-2 7299-58-3 41029-46-3 186494-67-7 186494-68-8
459832-21-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(aza-enediynes and aza-enyne allenes and aza-diallenes as DNA-cleaving antitumor agents)
IT 1123-99-5P 13141-42-9P 16344-79-9P 34657-82-4P 49572-60-3P
54624-57-6P 69045-24-5P 69696-00-0P 86521-05-3P 161885-73-0P
186494-69-9P 220079-65-2P 321200-63-9P 362604-08-8P 362604-13-5P
362604-45-3P 362604-48-6P 362604-49-7P 362604-50-0P 459832-17-8P
459832-23-6P 459832-24-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(aza-enediynes and aza-enyne allenes and aza-diallenes as DNA-cleaving antitumor agents)
IT 321200-62-8P 362604-46-4P 362604-47-5P 363134-54-7P 363134-55-8P
459832-22-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(aza-enediynes and aza-enyne allenes and aza-diallenes as DNA-cleaving antitumor agents)
IT **35070-01-0P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(aza-enediynes and aza-enyne allenes and aza-diallenes as DNA-cleaving antitumor agents)
RN 35070-01-0 HCAPLUS
CN Thiazole, 2-(phenylethynyl)- (9CI) (CA INDEX NAME)



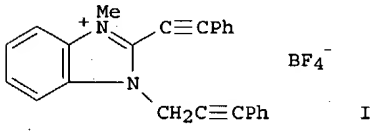
L52 ANSWER 2 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:721442 HCAPLUS
DN 135:272958
ED Entered STN: 03 Oct 2001
TI Preparation of aza-enediynes, aza-enyne allenes, or aza-diallenes as DNA-cleaving antitumor agents
IN Kerwin, Sean Michael; David, Wendi M.; Kumar, Dalip
PA Research Development Foundation, USA
SO U.S., 59 pp., Cont.-in-part of U.S. Ser. No. 356,303.
CODEN: USXXAM
DT Patent
LA English
IC ICM A61K031-13
NCL 514638000
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
Section cross-reference(s): 1, 27
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6297284	B1	20011002	US 2000-533723	20000323 <--
	WO 2001070217	A1	20010927	WO 2001-US9334	20010322
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 2002132797	A1	20020919	US 2001-967133	20010928 <--
	US 6686345	B2	20040203		
PRAI	US 1998-93112P	P	19980716	<--	
	US 1999-356303	A2	19990716	<--	
	US 2000-533723	A	20000323		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6297284	ICM	A61K031-13
	NCL	514638000

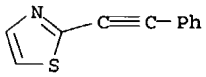
OS MARPAT 135:272958
GI



I

AB A chemical composition and method of use of the composition is described. The chemical composition includes an aza-enediyne, aza-enyne allene, or an aza-diallene. These compound are preferably non-hydrolyzable, cationic compds. that bind to nucleic acids. In addition it is believed that these compds. may undergo chemical reactions in the presence of a nucleic acid to generate reactive intermediates that cleave nucleic acids. E.g., AZB-002 (I) was prepared
ST aza enediyne prepn DNA cleaving antitumor agent; enyne allene aza prepn DNA cleaving antitumor agent; diallene aza prepn DNA cleaving antitumor agent; DNA cleaving antitumor agent aza enyne
IT Allenes
Enediynes
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aza-; preparation of aza-enediynes, aza-enyne allenes, or aza-diallenes as DNA-cleaving antitumor agents)

IT Antitumor agents
(preparation of aza-enediynes, aza-enyne allenes, or aza-diallenes as DNA-cleaving antitumor agents)
IT DNA
RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)
(preparation of aza-enediynes, aza-enyne allenes, or aza-diallenes as DNA-cleaving antitumor agents)
IT 37536-65-5P 321200-63-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of aza-enediynes, aza-enyne allenes, or aza-diallenes as DNA-cleaving antitumor agents)
IT 186494-69-9P 186494-70-2P 255716-41-7P 321200-62-8P 321200-65-1P
321200-67-3P 362604-49-7P 363134-45-6P 363134-46-7P 363134-47-8P
363134-48-9P 363134-49-0P 363134-51-4P 363134-53-6P 363134-54-7P
363134-55-8P 363134-56-9P 363134-57-0P 363134-58-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aza-enediynes, aza-enyne allenes, or aza-diallenes as DNA-cleaving antitumor agents)
IT 95-54-5, o-Phenylenediamine, reactions 109-04-6, 2-Bromopyridine
136-95-8, 2-Benzothiazolamine 536-74-3, Phenylacetylene 583-39-1
668-94-0 766-97-2, p-Tolylacetylene 1066-54-2, Trimethylsilylacetylene
2579-22-8, 3-Phenylpropynal 3034-53-5 4440-01-1, Lithium phenylacetylide 4595-60-2, 2-Bromopyrimidine 7299-58-3 23402-78-0
41029-46-3 77242-15-0 89343-06-6, Triisopropylsilylacetylene
255716-39-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of aza-enediynes, aza-enyne allenes, or aza-diallenes as DNA-cleaving antitumor agents)
IT 1123-99-5P 13141-42-9P 34657-82-4P **35070-01-0P** 49572-60-3P
54624-57-6P 69045-24-5P 69696-00-0P 161885-73-0P 201489-34-1P
220079-65-2P 255390-20-6P 255390-21-7P 255390-22-8P 255390-23-9P
325793-43-9P 362604-08-8P 362604-11-3P 362604-13-5P 362604-45-3P
362604-46-4P 362604-48-6P 362604-50-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aza-enediynes, aza-enyne allenes, or aza-diallenes as DNA-cleaving antitumor agents)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Bunten; Macromolecules 1996, V29, P2885 HCAPLUS
(2) Kouvetakis; Chem Mater 1994, V6, P636 HCAPLUS
(3) Lavoie; US 5767142 1998 HCAPLUS
IT **35070-01-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of aza-enediynes, aza-enyne allenes, or aza-diallenes as DNA-cleaving antitumor agents)
RN 35070-01-0 HCAPLUS
CN Thiazole, 2-(phenylethynyl)- (9CI) (CA INDEX NAME)



L52 ANSWER 3 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2001:713131 HCAPLUS
DN 135:267214
ED Entered STN: 28 Sep 2001
TI Aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents
IN Kerwin, Sean Michael; David, Wendi M.; Kumar, Dalip
PA Research Development Foundation, USA
SO PCT Int. Appl., 115 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM A61K031-13

ICS A61K031-415
CC 1-6 (Pharmacology)
Section cross-reference(s): 25, 27, 28, 63
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001070217	A1	20010927	WO 2001-US9334	20010322
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6297284	B1	20011002	US 2000-533723	20000323 <--
PRAI	US 2000-533723	A	20000323		
	US 1998-93112P	P	19980716 <--		
	US 1999-356303	A2	19990716 <--		

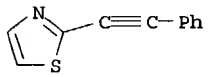
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001070217	ICM	A61K031-13
	ICS	A61K031-415

OS MARPAT 135:267214
AB A chemical composition and method of use of the composition is described. The chemical composition includes an aza-enediyne, aza-enyne allene, or an aza-diallene. These compds. are preferably non-hydrolyzable, cationic compds. that bind to nucleic acids. In addition it is believed that these compds. may undergo chemical reactions in the presence of a nucleic acid to generate reactive intermediates that cleave nucleic acids. Compound preparation is described.
ST azaenediyne DNA cleaving antitumor agent prepn; azaenyne allene DNA cleaving antitumor agent prepn; azadiallene DNA cleaving antitumor agent prepn
IT Intercalation
(agents, nucleic acid-interactive; aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
IT Glycosides
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(amino, nucleic acid-interactive; aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
IT Peptides, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(and peptoids, nucleic acid-interactive; aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
IT Alkylating agents, biological
Antitumor agents
Drug delivery systems
Metalation
(aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
IT Biradicals
DNA
Nucleic acids
RNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
IT DNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(cleavage; aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
IT Onium compounds
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(iminium; aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
IT Antitumor agents
(lung non-small-cell carcinoma, A549 cell; aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)

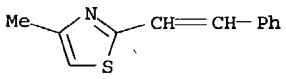
IT Antitumor agents
(lymphoma; aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
IT Gene, animal
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(mdm-2; aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
IT Lung, neoplasm
(non-small-cell carcinoma, inhibitors, A549 cell; aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
IT Carbohydrates, biological studies
Crown ethers
Oligonucleotides
Oligosaccharides, biological studies
Peptide nucleic acids
Porphyrins
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(nucleic acid-interactive; aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
IT 325793-43-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
IT 362604-18-0P 362604-21-5P 362604-26-0P 362604-30-6P 362604-32-8P 362604-35-1P 362604-37-3P 363134-47-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
IT 37536-65-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
IT 186494-68-8P 186494-69-9P 255716-41-7P 362604-40-8P 362604-44-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
IT 321200-65-1 362604-39-5 362604-42-0
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
IT 220079-65-2P 362604-08-8P 362604-11-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
IT 260359-31-7P 362604-46-4P 362604-47-5P 362604-49-7P 362604-50-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
IT **35070-01-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
IT 13141-42-9P 49572-60-3P 54624-57-6P 69696-00-0P 161885-73-0P 186494-63-3P 186494-66-6P 186494-72-4P 321200-63-9P 362604-13-5P 362604-45-3P 362604-48-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and reaction; aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
IT 362604-15-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(reaction; aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
IT 95-54-5, 1,2-Benzenediamine, reactions 98-59-9 109-04-6 124-63-0, Methanesulfonyl chloride 136-95-8, 2-Benzothiazolamine 431-47-0 536-74-3 583-39-1 766-97-2 1066-54-2 1123-99-5 2579-22-8 3034-53-5 4440-01-1 4595-60-2 7299-58-3 7556-82-3 23402-78-0 24424-99-5 34657-82-4 69045-24-5 77242-15-0 89343-06-6 186494-67-7 255716-39-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction; aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Bunten; Macromolecules 1996, V29(8), P2885 HCAPLUS
(2) Kouvetakis; Chem Mater 1994, V6(5), P636 HCAPLUS
(3) La Voie; US 5767142 A 1998 HCAPLUS
IT **35070-01-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction; aza-enediyne, aza-enyne allene, and aza-diallene DNA-cleaving antitumor agents)
RN 35070-01-0 HCAPLUS
CN Thiazole, 2-(phenylethynyl)- (9CI) (CA INDEX NAME)



L52 ANSWER 4 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 2000:276336 HCAPLUS
DN 133:17553
ED Entered STN: 28 Apr 2000
TI Additional cycle formation from 2-dialkoxyphosphonylmethylthiazole
AU Baimashev, B. A.; Polezhaeva, N. A.; Klimovitskii, E. N.
CS A.M.Butlerov Research Chemical Institute, Kasan State University, Kasan, 420008, Russia
SO Phosphorus, Sulfur and Silicon and the Related Elements (1998), 132, 251-257
CODEN: PSSLEC; ISSN: 1042-6507
PB Gordon & Breach Science Publishers
DT Journal
LA English
CC 29-7 (Organometallic and Organometalloidal Compounds)
Section cross-reference(s): 28
OS CASREACT 133:17553
AB Diisopropoxyphosphonyl-2-(4-methylthiazolyl)methane reacts with carbonyl and .alpha.-halocarbonyl compds. by three routes. In the case of Knoevenagel or Horner-Wadsworth-Emmons reactions the corresponding ethylenes were produced, whereas employing .alpha.-halocarbonyls as partners resulted in pyrrolo[2.1b]thiazoles. 1-Phosphonyl-1-(2-thiazolyl)-ethylene undergoes smoothly [4+2] and [3+2] cycloaddn. reactions.
ST alkoxy phosphonylmethyl thiazole Knoevenagel Horner Wadsworth Emmons reaction; carbonyl halocarbonyl compd reaction diisopropoxyphosphonyl methylthiazolyl methane; phosphonyl thiazolyl ethylene cycloaddn reaction; pyrrolo thiazole prepn
IT Horner Wadsworth Emmons reaction
Knoevenagel reaction
(of diisopropoxyphosphonyl methylthiazolyl methane)
IT Cycloaddition reaction
(of phosphonyl thiazolyl ethylene)
IT 169828-37-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(cycloaddn. reaction of)
IT 542-92-7, Cyclopentadiene, reactions 6832-16-2, Methyl diazoacetate

RL: RCT (Reactant); RACT (Reactant or reagent)
(cycloaddn. reaction with phosphonyl thiazolyl ethylene)
IT 272790-63-3P 272790-64-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and cyclization of)
IT **24622-44-4P** 272790-59-7P 272790-60-0P 272790-61-1P
272790-62-2P 272790-65-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
IT 148901-76-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with carbonyl and halocarbonyl compds.)
IT 70-11-1, Phenacyl bromide 100-52-7, Benzaldehyde, reactions 598-31-2, Bromoacetone
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with diisopropoxyphosphonyl methylthiazolyl methane)
IT 110-89-4, Piperidine, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with thiazolium salt)
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; The chemistry of heterocyclic compounds 1956
(2) Baimashev, B; Zhur Obshch Khim 1995, V65, P522 HCAPLUS
(3) Baimashev, B; Zhur: Obshch Khim 1993, V63, P219 HCAPLUS
(4) Corey, E; Tetrahedron Lett 1976, P4041
(5) Dondoni, A; Tetrahedron 1988, V44, P2021 HCAPLUS
(6) Mikolajczyk, M; Tetrahedron: Asymmetry 1992, V3, P1515 HCAPLUS
(7) Minami, T; Phosphorus, Sulfur and Silicon 1993, V75, P135 HCAPLUS
(8) Nugent, R; J Med Chem 1993, V36, P134 HCAPLUS
(9) Page, P; Phosphorus, Sulfur and Silicon 1992, V70, P205 HCAPLUS
(10) Sturtz, G; Eur J Med Chem 1992, V27, P825 HCAPLUS
(11) Sturtz, G; Eur J Med Chem 1993, V28, P899 HCAPLUS
(12) Vernin, G; The Chemistry of Heterocyclic Compounds, Part III: General Synthetic Methods for Thiazole and Thiazolium Salts 1979, V34, P165 HCAPLUS
IT **24622-44-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 24622-44-4 HCAPLUS
CN Thiazole, 4-methyl-2-(2-phenylethenyl)- (9CI) (CA INDEX NAME)



L52 ANSWER 5 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:213402 HCAPLUS
DN 125:247714
ED Entered STN: 13 Apr 1996
TI An unusual dependency of counterion during Wittig methylenation of bisheteroaryl ketones. [Erratum to document cited in CA124:175972]
AU Subramanyam, C.
CS Dep. Medicinal Chemistry, Sanofi Research Div., Malvern, PA, 19355, USA
SO Tetrahedron Letters (1996), 37(14), 2315
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier
DT Journal
LA English
CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
AB Fig. 7a-c is corrected The errors were not reflected in the abstract or the index entries.
ST erratum Wittig methylenation bisheteroaryl ketone counterion; Wittig methylenation bisheteroaryl ketone counterion erratum; methylenation bisheteroaryl ketone counterion effect erratum; methylphosphonium bromide Wittig heteroaryl ketone erratum
IT Wittig reaction
(dependency of counterion during Wittig methylenation of bis-heteroaryl ketones (Erratum))
IT Ketones, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(dependency of counterion during Wittig methylenation of bis-heteroaryl ketones (Erratum))
IT 173730-26-2P

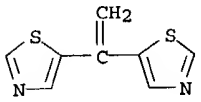
RL: BYP (Byproduct); PREP (Preparation)
(dependency of counterion during Wittig methylenation of bis-heteroaryl ketones (Erratum))

IT 1779-49-3, Methyltriphenylphosphonium bromide 19437-26-4, Bis(2-pyridyl)ketone 55707-55-6 161227-64-1 162468-75-9 169377-36-0 169378-49-8 170486-73-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(dependency of counterion during Wittig methylenation of bis-heteroaryl ketones (Erratum))

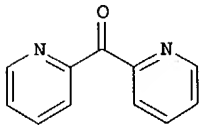
IT 54416-76-1P 115201-42-8P 161227-65-2P **161227-87-8P** 170486-63-2P 173730-27-3P 173730-28-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(dependency of counterion during Wittig methylenation of bis-heteroaryl ketones (Erratum))

IT **161227-87-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(dependency of counterion during Wittig methylenation of bis-heteroaryl ketones (Erratum))

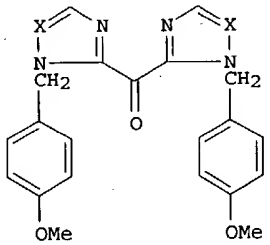
RN 161227-87-8 HCAPLUS
CN Thiazole, 5,5'-ethenylidenebis- (9CI) (CA INDEX NAME)



L52 ANSWER 6 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1996:5391 HCAPLUS
DN 124:175972
ED Entered STN: 02 Jan 1996
TI An unusual dependency of counterion during Wittig methylenation of bis-heteroaryl ketones
AU Subramanyam, Chakrapani
CS Dep. Medicinal Chemistry, Sanofi Research Div., Malvern, PA, 19355, USA
SO Tetrahedron Letters (1995), 36(51), 9249-52
CODEN: TELEAY; ISSN: 0040-4039
PB Elsevier
DT Journal
LA English
CC 28-10 (Heterocyclic Compounds (More Than One Hetero Atom))
OS CASREACT 124:175972
GI



I



II

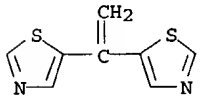
AB Attempted Wittig methylenation of some bis-heteroarom. ketones, e.g. I and II (X = N, CH), using MeP+Ph3Br- and n-BuLi gave none of the desired olefin. However, when tBuOK was used as the base for generation of the ylide, efficient olefination of these ketones was observed A possible mechanistic pathway for this interesting but unprecedented observation is proposed.

ST Wittig methylenation bisheteroaryl ketone counterion effect; methylphosphonium bromide Wittig heteroaryl ketone

IT Wittig reaction
(dependency of counterion during Wittig methylenation of bis-heteroaryl ketones)

IT Ketones, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)

(dependency of counterion during Wittig methylenation of bis-heteroaryl ketones)
IT 173730-26-2P
RL: BYP (Byproduct); PREP (Preparation)
(dependency of counterion during Wittig methylenation of bis-heteroaryl ketones)
IT 1779-49-3, Methyltriphenylphosphonium bromide 19437-26-4, Bis(2-pyridyl)ketone 55707-55-6 161227-64-1 162468-75-9 169377-36-0 169378-49-8 170486-73-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(dependency of counterion during Wittig methylenation of bis-heteroaryl ketones)
IT 54416-76-1P 115201-42-8P 161227-65-2P **161227-87-8P** 170486-63-2P 173730-27-3P 173730-28-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(dependency of counterion during Wittig methylenation of bis-heteroaryl ketones)
IT **161227-87-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(dependency of counterion during Wittig methylenation of bis-heteroaryl ketones)
RN 161227-87-8 HCAPLUS
CN Thiazole, 5,5'-ethenylidenebis- (9CI) (CA INDEX NAME)



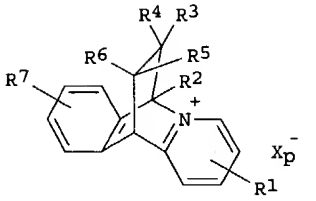
L52 ANSWER 7 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1995:928116 HCAPLUS
DN 123:339769
ED Entered STN: 18 Nov 1995
TI Preparation of 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA receptor antagonists
IN DeHaven-Hudkins, Diane L.; Dority, John A., Jr.; Earley, William G.; Kumar, Virendra; Mallamo, John P.; Miller, Matthew S.; Subramanyam, Chakrapani
PA Sterling Winthrop Inc., USA
SO Can. Pat. Appl., 220 pp.
CODEN: CPXXEB
DT Patent
LA English
IC ICM C07D455-00
ICS C07D519-00; C07F007-10; C07F009-547; A61K031-47; A61K031-495; A61K031-535; A61K031-675; A61K031-695
CC 27-18 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	CA 2131966	AA	19950315	CA 1994-2131966	19940913 <--
	US 5554620	A	19960910	US 1994-283317	19940729 <--
PRAI	US 1993-121127		19930914 <--		
	US 1994-283317		19940729 <--		

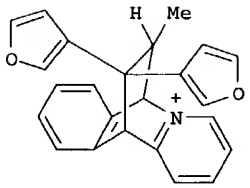
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
CA 2131966	ICM	C07D455-00
	ICS	C07D519-00; C07F007-10; C07F009-547; A61K031-47; A61K031-495; A61K031-535; A61K031-675; A61K031-695

OS MARPAT 123:339769
GI



I



II

AB Title compds. (I; R1,R7 = H, halo, alkyl, alkoxy, etc.; R2 = H, alkyl, cyano, alkoxycarbonyl; R3,R4 = H, alkyl; R3R4 = alkylidene, alkylene; R5,R6 = Ph, heteroaryl, heterocyclyl, etc.; R3R5,R4R6 = atoms to form a bicyclic ring system; X- = anion; p = 0 when R7 is neg. charged; p = 1 when R7 is not neg. charged) were prepared Thus, 1,1-bis(3-furyl)propene was cyclocondensed with benzo[b]quinolizinium hexafluorophosphate (preparation each given) to give, as 1 of 2 regioisomers, title compound II which had IC50 of 11.4nM against NMDA-induce neurotoxicity in cultured neurons in vitro.

ST benzoquinolizinium ethanodihydro NMDA receptor antagonist

IT Nervous system
(disease, degeneration, treatment; preparation of 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA receptor antagonists)

IT Toxicity
(neurotoxicity, treatment; preparation of 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA receptor antagonists)

IT 170484-90-9P 170484-91-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA receptor antagonists)

IT 161227-90-3P 170484-21-6P 170484-23-8P 170484-34-1P 170484-41-0P
170484-46-5P 170484-49-8P 170484-53-4P 170484-56-7P 170484-58-9P
170484-63-6P 170484-66-9P 170484-71-6P 170484-74-9P 170484-76-1P
170484-81-8P 170484-83-0P 170484-85-2P 170484-88-5P 170484-93-2P
170484-94-3P 170484-97-6P 170485-00-4P 170485-03-7P 170485-05-9P
170485-07-1P 170485-10-6P 170485-17-3P 170485-19-5P 170485-26-4P
170485-27-5P 170485-31-1P 170485-34-4P 170485-37-7P 170485-40-2P
170485-43-5P 170485-48-0P 170485-51-5P 170485-61-7P 170485-66-2P
170485-69-5P 170485-77-5P 170485-81-1P 170485-84-4P 170485-88-8P
170485-93-5P 170485-97-9P 170485-99-1P 170486-02-9P 170486-06-3P
170486-11-0P 170486-18-7P 170486-37-0P 170714-32-6P 170714-33-7P
170714-70-2P 170897-48-0P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA receptor antagonists)

IT 161227-46-9P 161227-47-0P 161227-48-1P 161227-49-2P 161227-51-6P
161227-53-8P 161227-54-9P 161227-68-5P 161227-69-6P 161227-70-9P
161227-71-0P 161227-72-1P 161227-73-2P 161227-74-3P 161227-76-5P
161227-78-7P 161227-80-1P 161227-81-2P 161227-82-3P 161227-83-4P
170484-13-6P 170484-15-8P 170484-17-0P 170484-19-2P 170484-25-0P
170484-27-2P 170484-29-4P 170484-30-7P 170484-32-9P 170484-37-4P
170484-39-6P 170484-42-1P 170484-44-3P 170484-47-6P 170484-50-1P
170484-51-2P 170484-54-5P 170484-60-3P 170484-61-4P 170484-64-7P
170484-67-0P 170484-69-2P 170484-72-7P 170484-77-2P 170484-78-3P
170484-79-4P 170484-86-3P 170484-89-6P 170484-95-4P 170484-98-7P
170485-01-5P 170485-08-2P 170485-11-7P 170485-13-9P 170485-15-1P
170485-20-8P 170485-22-0P 170485-24-2P 170485-29-7P 170485-32-2P
170485-35-5P 170485-38-8P 170485-41-3P 170485-45-7P 170485-46-8P
170485-49-1P 170485-52-6P 170485-54-8P 170485-56-0P 170485-58-2P
170485-59-3P 170485-62-8P 170485-63-9P 170485-64-0P 170485-67-3P
170485-70-8P 170485-71-9P 170485-72-0P 170485-73-1P 170485-75-3P
170485-78-6P 170485-79-7P 170485-82-2P 170485-85-5P 170485-86-6P
170485-89-9P 170485-91-3P 170485-94-6P 170485-95-7P 170486-00-7P
170486-03-0P 170486-04-1P 170486-08-5P 170486-09-6P 170486-12-1P
170486-14-3P 170486-15-4P 170486-16-5P 170486-19-8P 170486-21-2P
170486-23-4P 170486-24-5P 170486-26-7P 170486-27-8P 170486-29-0P
170486-31-4P 170486-95-0P 170714-30-4P 170714-31-5P 170714-35-9P

170714-37-1P 170714-39-3P 170714-41-7P 170714-42-8P 170714-43-9P
170714-45-1P 170714-47-3P 170714-49-5P 170714-51-9P 170714-53-1P
170714-55-3P 170714-57-5P 170714-59-7P 170714-61-1P 170714-63-3P
170714-64-4P 170714-66-6P 170714-68-8P 170714-71-3P 170714-73-5P
170897-45-7P 170897-46-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA receptor antagonists)

IT 75-26-3, Isopropyl bromide 78-95-5, Chloroacetone 79-31-2, Isobutyric acid 83-33-0, 1-Indanone 90-96-0, Di-(4-methoxyphenyl) ketone 90-98-2, Di-(4-chlorophenyl) ketone 95-13-6, Indene 100-11-8, 4-Nitrobenzyl bromide 100-39-0, Benzyl bromide 100-83-4, 3-Hydroxybenzaldehyde 107-19-7, Propargyl alcohol 108-86-1, Bromobenzene, reactions 110-00-9, Furan 111-64-8, Octanoyl chloride 111-83-1, Octyl bromide 111-87-5, 1-Octanol, reactions 119-61-9, Benzophenone, reactions 119-84-6 271-89-6, Benzofuran 288-42-6, Oxazole 329-15-7, 4-Trifluoromethylbenzoyl chloride 345-92-6 372-47-4, 3-Fluoropyridine 459-46-1, 4-Fluorobenzyl bromide 486-25-9, 9-Fluorenone 486-73-7, 1-Isoquinolinecarboxylic acid 488-93-7, Furan-3-carboxylic acid 495-76-1, 3,4-Methylenedioxybenzyl alcohol 527-72-0, Thiophene-2-carboxylic acid 530-48-3, 1,1-Diphenylethylene 586-37-8 591-51-5, Phenyllithium 611-97-2, Di-(p-tolyl) ketone 614-98-2, Ethyl 3-furoate 615-59-8, 2,5-Dibromotoluene 615-74-7, 2-Chloro-5-methylphenol 626-05-1, 2,6-Dibromopyridine 626-55-1, 3-Bromopyridine 778-66-5, 1,1-Diphenyl-1-propene 824-94-2, 4-Methoxybenzyl chloride 872-31-1, 3-Bromothiophene 1003-67-4, 4-Picoline N-oxide 1121-60-4, 2-Pyridinecarboxaldehyde 1122-72-1 1849-53-2 1868-00-4, 3,3'-Bis(trifluoromethyl)benzophenone 1929-29-9, 3-(4-Methoxyphenyl)propionic acid 2398-37-0, 3-Bromoanisole 2743-38-6, Dibenzoyl-L-tartaric acid 3034-53-5, 2-Bromothiazole 3042-81-7, Methyl .alpha.-bromophenylacetate 6126-10-9, 1-(p-Toluenesulfonyl)pyrazole 6630-33-7, 2-Bromobenzaldehyde 6971-51-3, 3-Methoxybenzyl alcohol 7094-34-0, Di-(3-chlorophenyl) ketone 10599-70-9 13414-95-4 14114-05-7, Cyclopropyl triphenylphosphonium bromide 14794-31-1 16806-93-2, 4,5,6,7-Tetrahydrobenzofuran-4-one 17026-42-5, Dibenzoyl-D-tartaric acid 18595-18-1 19524-06-2, 4-Bromopyridine hydrochloride 22037-28-1, 3-Bromofuran 25032-74-0 27104-73-0, Methyl 3-isoquinolinecarboxylate 33524-31-1, 2,5-Dimethoxybenzyl alcohol 39193-85-6 54416-76-1, 1,1-Bis(2-pyridyl)ethene 56643-95-9, 1-(4-Methoxybenzyl)imidazole 62456-33-1 67088-76-0, Di-(4-pyrazolyl) ketone 73942-52-6 79265-30-8, 2-(Trimethylsilyl)thiazole 91272-98-9 97407-07-3 108153-93-1, 4,5,6,7-Tetrahydrobenzofuran-7-one 131674-46-9 133560-57-3 141776-91-2, 3,5-Difluorobenzyl bromide 145162-51-2, 1-(4-Methoxybenzyl)pyrazole 168886-97-3 170487-35-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA receptor antagonists)

IT 349-95-1P, 4-(Trifluoromethyl)benzyl alcohol 402-49-3P, 4-(Trifluoromethyl)benzyl bromide 704-38-1P, Di-(2-thienyl) ketone 1120-87-2P, 4-Bromopyridine 1488-34-2P, 1,1-Bis(3-methoxyphenyl)ethene 1586-16-9P 1586-54-5P 1695-36-9P 1695-37-0P 1695-38-1P 1961-96-2P, 1-Phenylindene 2642-81-1P, 1,1-Bis(4-chlorophenyl)ethene 2919-20-2P, 1,1-Bis(4-methylphenyl)ethene 4356-69-8P, 1,1-Bis(4-methoxyphenyl)ethene 4425-82-5P, 9-Methylenefluorene 4494-18-2P, 1-Isoquinolinecarboxaldehyde 5470-80-4P, 3-Isoquinolinecarboxaldehyde 5693-54-9P 6175-14-0P, 1,1-Bis(4-fluorophenyl)ethene 6918-15-6P, Di-(4-pyridyl) ketone 7547-88-8P, Benzo[b]quinolizinium bromide 7547-93-5P 7632-57-7P, (Diphenylmethylene)cyclopropane 10605-43-3P, 1,1-Bis(4-bromophenyl)ethene 10605-50-2P 13336-31-7P, 4-Methoxy-1-indanone 13623-25-1P, 6-Methoxy-1-indanone 13726-17-5P 17920-86-4P, Di-(2-furyl) ketone 20583-35-1P, Di-(5-pyrazolyl) ketone 23308-82-9P, 3-Methoxy-.alpha.-methylbenzyl alcohol 26066-15-9P 26453-81-6P, Di-(3-thienyl) ketone 27104-72-9P, Methyl 1-isoquinolinecarboxylate 27755-38-0P 29265-85-8P, 1,1-Bis(3-bromophenyl)ethene 30078-67-2P, 1-(3-Furyl)-1-propanone 30782-41-3P, 1,1-Bis(2-thienyl)ethene 31224-43-8P 31794-11-3P 31936-92-2P, Di-(3-thienyl)methanol 32980-28-2P 34160-40-2P 35779-35-2P, Di-(3-pyridyl) ketone 38674-98-5P 40731-98-4P, 4-Hydroxy-1-indanone 42772-87-2P 50585-79-0P 53547-60-7P, 4-Methylpyridine-2-carboxaldehyde 54356-08-0P 55707-55-6P, Di-(2-thiazolyl) ketone 71255-11-3P 71721-60-3P 73909-16-7P, 2-Chloro-5-methylanisole 74808-20-1P 75792-33-5P, 3-Isopropoxybenzaldehyde 85740-98-3P 87630-36-2P 97360-71-9P 97437-74-6P 98946-66-8P, 1,1-Bis(3-thienyl)ethene 104053-68-1P

105399-18-6P, 1,1-Bis(2-furyl)ethene 112625-92-0P 115201-42-8P, 1-(4-Methoxybenzyl)-1,2,4-triazole 118994-84-6P, 4-Oxazolecarboxaldehyde 127158-63-8P 130551-90-5P 131674-48-1P 136105-40-3P 147643-74-1P 148900-66-7P 155855-38-2P, 1,1-Bis(3-trifluoromethylphenyl)ethene 156600-09-8P, Benzo[b]quinolizinium hexafluorophosphate 156841-32-6P 161227-55-0P 161227-56-1P 161227-57-2P 161227-60-7P 161227-61-8P 161227-63-0P 161227-64-1P 161227-65-2P 161227-84-5P, 1,1-Bis(3-pyridyl)ethene 161227-85-6P, 1,1-Bis(4-pyridyl)ethene 161227-86-7P, 1,1-Bis(3-furyl)ethene **161227-87-8P**, 1,1-Bis(5-thiazolyl)ethene 161227-88-9P 162468-75-9P 163190-83-8P 163190-85-0P 163190-87-2P 163190-91-8P 163190-93-0P 163190-99-6P 166886-01-7P 166886-03-9P 167165-98-2P 167166-00-9P 167166-38-3P 168886-66-6P 168886-69-9P 168886-71-3P 168886-73-5P 168886-75-7P 168886-77-9P 168886-79-1P 168886-80-4P 168886-81-5P 168886-82-6P 168886-83-7P 168886-87-1P 168886-89-3P 168886-90-6P 168886-92-8P 168886-98-4P 168887-00-1P 168887-02-3P 168887-04-5P 168887-08-9P 169377-19-9P 169377-20-2P 169377-21-3P 169377-22-4P 169377-23-5P 169377-25-7P 169377-26-8P 169377-27-9P 169377-28-0P 169377-29-1P 169377-33-7P 169377-34-8P 169377-36-0P 169377-39-3P 169377-40-6P 169377-93-9P 169378-38-5P, 1-Phenyl-6-methoxyindene 169378-40-9P, 1-Phenyl-4-methoxyindene 169378-42-1P, 1-(3-Methoxyphenyl)indene 169378-44-3P, 1-(3-Furyl)indene 169378-45-4P, 4-Ethoxy-6,7-dihydrobenzofuran 169378-46-5P, 1-(3-Furyl)-1-ethoxyethylene 169378-49-8P, Di-(5-thiazolyl) ketone 170486-32-5P 170486-33-6P 170486-34-7P 170486-38-1P 170486-39-2P 170486-40-5P 170486-41-6P 170486-43-8P 170486-45-0P 170486-47-2P 170486-48-3P 170486-49-4P 170486-50-7P 170486-51-8P 170486-53-0P 170486-54-1P 170486-55-2P 170486-57-4P 170486-58-5P 170486-59-6P 170486-61-0P 170486-62-1P 170486-63-2P 170486-65-4P 170486-67-6P 170486-69-8P 170486-70-1P 170486-71-2P 170486-72-3P 170486-73-4P 170486-74-5P 170486-75-6P 170486-76-7P 170486-78-9P 170486-79-0P 170486-80-3P 170486-81-4P 170486-83-6P 170486-84-7P 170486-85-8P 170486-87-0P 170486-88-1P 170486-90-5P 170486-91-6P 170486-93-8P 170486-97-2P 170486-98-3P 170486-99-4P 170487-00-0P 170487-01-1P 170487-02-2P 170487-04-4P 170487-05-5P 170487-06-6P 170487-07-7P 170487-08-8P 170487-09-9P 170487-10-2P 170487-12-4P 170487-14-6P 170487-16-8P 170487-17-9P 170487-19-1P 170487-21-5P 170487-22-6P 170487-23-7P 170487-24-8P 170487-25-9P 170487-26-0P 170487-27-1P 170487-29-3P 170487-30-6P 170487-32-8P 170487-34-0P 170487-36-2P, Monopotassium monobenzoyl-L-tartrate 170487-37-3P, Monopotassium monobenzoyl-D-tartrate 170487-38-4P, Methyl 4-oxazolecarboxylate 170487-39-5P, 2-Cyano-4-methylpyridine N-oxide 170487-40-8P, Methyl indazole-6-carboxylate

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA receptor antagonists)

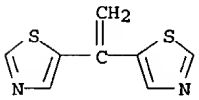
IT **161227-87-8P**, 1,1-Bis(5-thiazolyl)ethene

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of 6,11-ethano-6,11-dihydrobenzo[b]quinolizinium salts as NMDA receptor antagonists)

RN 161227-87-8 HCAPLUS

CN Thiazole, 5,5'-ethenylidenebis- (9CI) (CA INDEX NAME)



L52 ANSWER 8 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1995:283984 HCAPLUS

DN 123:83185

ED Entered STN: 10 Jan 1995

TI Discovery of 6,11-Ethano-12,12-diaryl-6,11-dihydrobenzo[b]quinolizinium Cations, a Novel Class of N-Methyl-D-aspartate Antagonists

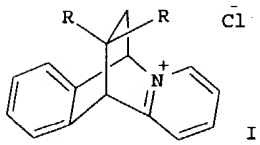
AU Subramanyam, Chakrapani; Mallamo, John P.; Dority, John A., Jr.; Earley, William G.; Kumar, Virendra; Aimone, Lisa D.; Ault, Brian; Miller, Matthew S.; Luttinger, Daniel A.; DeHaven-Hudkins, Diane L.

CS Department of Medicinal Chemistry, Sterling Winthrop Pharmaceuticals Research Division, Collegeville, PA, 19426-0900, USA

SO Journal of Medicinal Chemistry (**1995**), 38(1), 21-7

CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society
DT Journal
LA English
CC 27-18 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 1, 2
GI



I

AB 6,11-Ethano-12,12-diaryl-6,11-dihydrobenzo[b]quinolizinium cations, a novel class of N-methyl-D-aspartate (NMDA) antagonists acting at the phencyclidine site, have been identified. Structure-activity relationship studies around the lead compound I (R = Ph) led to the identification of I (R = 3-furyl) (WIN 67870-2), one of the most potent compds. in this series. I (R = 3-furyl) has a Ki = 1.8 .+-. 0.2 nM vs [3H]TCP binding, has 700-fold selectivity for binding to the open state of the NMDA receptor-ionophore, and was devoid of MK-801- and PCP-like behavioral effects in rats. I (R = 3-furyl) was neuroprotective in cultured mouse cortical neurons and exhibited antiischemic activity in a rat middle cerebral artery occlusion/reperfusion model of focal ischemia.

ST ethanobenzoquinolizinium diaryl prepn methylaspartate antagonist; diarylethanobenzoquinolizinium prepn methylaspartate antagonist

IT Molecular structure-biological activity relationship
(glutamatergic receptor-binding, preparation of ethanodiaryldihydrobenzoquinolizinium cations as novel methylaspartate antagonists)

IT Receptors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(glutamatergic, methyl-D-aspartate-binding, preparation of ethanodiaryldihydrobenzoquinolizinium cations as novel methylaspartate antagonists)

IT 6384-92-5, Nmda
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(preparation of ethanodiaryldihydrobenzoquinolizinium cations as novel methylaspartate antagonists)

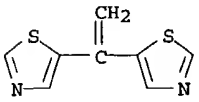
IT 161227-45-8P 161227-46-9P 161227-47-0P 161227-48-1P 161227-49-2P
161227-51-6P 161227-53-8P 161227-54-9P 161227-68-5P 161227-69-6P
161227-70-9P 161227-71-0P 161227-72-1P 161227-73-2P 161227-74-3P
161227-76-5P 161227-78-7P 161227-80-1P 161227-81-2P 161227-82-3P
161227-83-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of ethanodiaryldihydrobenzoquinolizinium cations as novel methylaspartate antagonists)

IT 1488-34-2 2642-81-1 4356-69-8 6175-14-0 6919-62-6 10605-43-3
10605-50-2 18507-95-4 29265-85-8 30782-41-3 54416-76-1
55707-55-6 56643-95-9 87630-36-2 98946-66-8 105399-18-6
133560-57-3 161227-84-5 161227-85-6 161227-86-7 **161227-87-8**
161227-88-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of ethanodiaryldihydrobenzoquinolizinium cations as novel methylaspartate antagonists)

IT 161227-55-0P 161227-56-1P 161227-57-2P 161227-59-4P 161227-60-7P
161227-61-8P 161227-63-0P 161227-64-1P 161227-65-2P 161227-67-4P
161227-90-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of ethanodiaryldihydrobenzoquinolizinium cations as novel methylaspartate antagonists)

IT **161227-87-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of ethanodiaryldihydrobenzoquinolizinium cations as novel

methylaspartate antagonists)
RN 161227-87-8 HCAPLUS
CN Thiazole, 5,5'-ethenylidenebis- (9CI) (CA INDEX NAME)



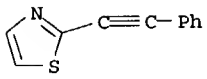
L52 ANSWER 9 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1992:214333 HCAPLUS
DN 116:214333
ED Entered STN: 31 May 1992
TI Preparation of (arylethynyl)heteroaromatics as acaricides and insecticides
IN Rentzea, Costin; Kardorff, Uwe; Kuenast, Christoph; Theobald, Hans; Kuekenhoener, Thomas
PA BASF A.-G., Germany
SO Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DT Patent
LA German
IC ICM C07D333-08
ICS C07D333-12; C07D333-16; C07D333-28; C07D277-22; A01N043-10; A01N043-78
CC 27-8 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 5
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 469411	A1	19920205	EP 1991-112154	19910720 <--
EP 469411	B1	19970611		
R: BE, CH, DE, DK, ES, FR, GB, IT, LI, NL				
DE 4024281	A1	19920206	DE 1990-4024281	19900731 <--
ES 2103759	T3	19971001	ES 1991-112154	19910720 <--
JP 04234381	A2	19920824	JP 1991-187421	19910726 <--
CA 2048159	AA	19920201	CA 1991-2048159	19910730 <--
US 5389656	A	19950214	US 1992-911386	19920713 <--
PRAI DE 1990-4024281		19900731 <--		
US 1991-737866		19910730 <--		

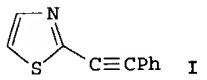
CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
EP 469411	ICM	C07D333-08
	ICS	C07D333-12; C07D333-16; C07D333-28; C07D277-22; A01N043-10; A01N043-78

OS MARPAT 116:214333
AB R1C.tplbond.CR2 [R1 = (substituted) heteroaryl; R2 = (substituted) (polycyclic) aryl] were prepared Thus, 2-bromothiophene was condensed with PhC.tplbond.CH to give 1-(2-thienyl)-2-phenylacetylene. 1-(3-Chloro-2-thienyl)-2-phenylacetylene gave 80-100% kill of Heliothis virescens larvae on bean leaves wetted with a 400-ppm preparation
ST heteroarom arylethynyl prepn acaricide insecticide
IT Acaricides
Insecticides
((arylethynyl)heteroaroms.)
IT 4805-17-8P **35070-01-0P** 131423-29-5P 140918-60-1P 140918-61-2P 140918-62-3P 140918-63-4P 140918-64-5P 140918-65-6P 140918-66-7P 140918-67-8P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as acaricide and insecticide)
IT 536-74-3, Phenylacetylene 1003-09-4, 2-Bromothiophene
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of acaricides and insecticides)
IT **35070-01-0P**
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of, as acaricide and insecticide)
RN 35070-01-0 HCAPLUS
CN Thiazole, 2-(phenylethynyl)- (9CI) (CA INDEX NAME)



L52 ANSWER 10 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1987:636598 HCAPLUS
DN 107:236598
ED Entered STN: 25 Dec 1987
TI Palladium-catalyzed reactions of terminal acetylenes and olefins with halo-1,3-azoles
AU Sakamoto, Takao; Nagata, Hideo; Kondo, Yoshinori; Shiraiwa, Masafumi; Yamanaka, Hiroshi
CS Pharm. Inst., Tohoku Univ., Sendai, 980, Japan
SO Chemical & Pharmaceutical Bulletin (1987), 35(2), 823-8
CODEN: CPBTAL; ISSN: 0009-2363
DT Journal
LA English
CC 28-9 (Heterocyclic Compounds (More Than One Hetero Atom))
OS CASREACT 107:236598
GI



I

AB The Pd-catalyzed reactions of 4-bromo- and 5-bromothiazoles, as well as 4-bromo- and 5-bromooxazoles with terminal acetylenes gave ethynyl derivs., e.g. I, in 43-89% yields, whereas the reactions of 2-bromothiazoles and iodo-N-methylimidazoles afforded the products in poor yields. The reaction of the halo-1,3-azoles with terminal olefins was also examined

ST thiazole alkynyl alkenyl; oxazole alkynyl alkenyl; imidazole alkynyl alkenyl; halothiazole alkynylation palladium catalyst; alkenylation haloazole palladium catalyst; heteroarom Heck arylation alkene alkyne

IT Alkenylation
Alkynylation
(of halooxazoles and halothiazoles)

IT Arylation
(Heck, of acetylenes and olefins with halooxazoles and halothiazoles)

IT 7007-07-0 20662-93-5 28771-82-6 34259-99-9 37067-95-1 57516-16-2 71759-87-0 71759-88-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkynylation and alkenylation of, in the presence of a palladium catalyst)

IT 3034-53-5 111600-83-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkynylation of, in the presence of a palladium catalyst)

IT 140-88-5, Ethyl acrylate 1066-54-2, (Trimethylsilyl)acetylene
RL: RCT (Reactant); RACT (Reactant or reagent)
(arylation of, with bromothiazoles and -oxazoles, palladium catalyzed)

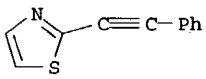
IT 536-74-3, Phenyl acetylene
RL: RCT (Reactant); RACT (Reactant or reagent)
(arylation of, with halothiazoles and -oxazoles, palladium catalyzed)

IT 1826-12-6P 1826-17-1P 4072-63-3P **35070-01-0P** 37570-94-8P 55384-94-6P 67879-31-6P 71759-92-7P 83247-14-7P 108905-60-8P 111600-84-1P 111600-85-2P 111600-86-3P 111600-87-4P **111600-88-5P** 111600-89-6P 111600-90-9P 111600-91-0P **111600-92-1P** 111600-93-2P 111600-94-3P 111600-95-4P 111600-96-5P 111600-97-6P 111600-98-7P 111600-99-8P 111601-00-4P 111601-01-5P 111601-02-6P 111601-03-7P 111601-04-8P 111601-05-9P 111601-06-0P 111601-07-1P 111601-08-2P 111601-09-3P 111601-10-6P 111601-11-7P 111601-12-8P 111601-13-9P 111601-14-0P 111601-15-1P 111601-16-2P 111601-17-3P 111620-41-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

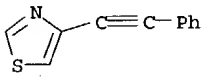
IT 107-13-1, Acrylonitrile, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with bromothiazoles and -oxazoles, palladium catalyzed)

IT 100-42-5, Styrene, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)

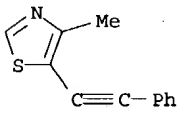
(reaction of, with halothiazoles and -oxazoles, palladium catalyzed)
IT **35070-01-0P 111600-88-5P 111600-92-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 35070-01-0 HCAPLUS
CN Thiazole, 2-(phenylethynyl)- (9CI) (CA INDEX NAME)



RN 111600-88-5 HCAPLUS
CN Thiazole, 4-(phenylethynyl)- (9CI) (CA INDEX NAME)



RN 111600-92-1 HCAPLUS
CN Thiazole, 4-methyl-5-(phenylethynyl)- (9CI) (CA INDEX NAME)



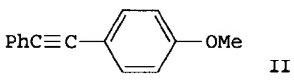
L52 ANSWER 11 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1982:117583 HCAPLUS
DN 96:117583
ED Entered STN: 12 May 1984
TI Soil disinfectant composition
PA Kanesho Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC A01N027-00; A01N029-00; A01N031-14; A01N043-06; A01N043-40; A01N043-78
CC 5-2 (Agrochemical Bioregulators)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 56154401	A2	19811130	JP 1980-58501	19800501 <--
JP 59028522	B4	19840713		
PRAI JP 1980-58501		19800501 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES		
JP 56154401	IC	A01N027-00IC	A01N029-00IC	A01N031-14IC
		A01N043-06IC	A01N043-40IC	A01N043-78

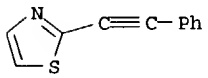
OS CASREACT 96:117583
GI



II

AB The compds. R1C.tplbond.CR2 (I; R1 and R2 = alkenyl, alkynyl, or aromatic) are soil disinfectants. The synthesis of I is given. Thus, 200 ppm of II [7380-78-1] at 3 L/m3 soil controlled Pythium aphanidermatum on cucumber.
ST soil disinfectant compn
IT Bactericides, Disinfectants, and Antiseptics
(preparation and activity of)
IT Fungicides and Fungistats
(soil disinfectant, preparation and activity of)
IT 886-66-8P 1206-02-6P 1463-04-3P 3287-02-3P 3725-09-5P 4805-17-8P

5701-81-5P 7380-78-1P 13141-42-9P 13295-94-8P 13295-97-1P
13456-84-3P 13633-26-6P 23975-15-7P 28790-65-0P **35070-01-0P**
35133-77-8P 49836-17-1P 49836-18-2P 50559-45-0P 55110-61-7P
65406-81-7P 80221-12-1P 80221-14-3P 80221-15-4P 80221-19-8P
80221-20-1P 80746-49-2P
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and microbicidal activity of)
IT 109-89-7, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with bromochlorohexane, in soil disinfectant manufacture)
IT 536-74-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with bromopropane, in soil disinfectant manufacture)
IT 696-62-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with phenylacetylene copper, in soil disinfectant manufacture)
IT 106-94-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with phenylacetylene, in soil disinfectant manufacture)
IT 1003-09-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with piperidine, in soil disinfectant manufacture)
IT **35070-01-0P**
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and microbicidal activity of)
RN 35070-01-0 HCAPLUS
CN Thiazole, 2-(phenylethynyl)- (9CI) (CA INDEX NAME)



L52 ANSWER 12 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1982:16085 HCAPLUS
DN 96:16085
ED Entered STN: 12 May 1984
TI Acetylene derivatives as nematocides
PA Kanesho Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
IC A01N027-00; A01N031-04; A01N031-08; A01N033-06; A01N033-18; A01N035-04; A01N037-18; A01N037-34; A01N043-06; A01N043-40; A01N043-78
CC 5-4 (Agrochemical Bioregulators)
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 56123903	A2	19810929	JP 1980-27155	19800304 <--
JP 59028521	B4	19840713		
PRAI JP 1980-27155		19800304 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES		
JP 56123903	IC	A01N027-00IC	A01N031-04IC	A01N031-08IC
		A01N033-06IC	A01N033-18IC	A01N035-04IC
		A01N037-18IC	A01N037-34IC	A01N043-06IC
		A01N043-40IC	A01N043-78	

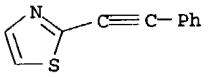
AB Acetylene derivs. are nematocides. The syntheses of such compds. are given. Thus, 500 .mu.M MeO2CCH:CH.cntdot.C.tplbond.C.cntdot.CH:CHCO2Me [28813-55-0] controlled Pratylenchus coffeae by 99.2% in 48 h.
ST acetylene nematocide
IT Nematocides
(acetylenes)
IT 886-66-8 959-88-6 1206-02-6 1223-47-8 1463-04-3 1820-42-4
1849-25-8 1849-26-9 1849-27-0 1942-30-9 2735-14-0 2789-88-0
2789-89-1 3287-02-3 3725-09-5 4805-17-8 5216-36-4 5293-78-7
5701-81-5 6775-17-3 7380-78-1 13141-38-3 13141-40-7 13141-41-8
13141-42-9 13141-44-1 13141-45-2 13295-94-8 13295-97-1

13456-84-3 13633-26-6 22666-07-5 23975-15-7 25407-11-8
25739-23-5 28790-65-0 28813-55-0 29768-12-5 30405-77-7
35010-17-4 **35070-01-0** 35133-77-8 41398-67-8 42296-34-4
49836-17-1 49836-18-2 49836-19-3 49836-21-7 50559-45-0
51118-06-0 54075-56-8 55110-61-7 55384-98-0 57341-98-7
59647-77-7 59672-51-4 61440-87-7 65406-81-7 74149-28-3
79135-69-6 80220-64-0 80220-65-1 80220-66-2 80221-08-5
80221-09-6 80221-10-9 80221-11-0 80221-12-1 80221-13-2
80221-14-3 80221-15-4 80221-16-5 80221-17-6 80221-18-7
80221-19-8 80221-20-1 80221-21-2 80221-22-3 80221-23-4
80221-24-5 80238-88-6
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study); USES (Uses)
(nematocide)

IT 74-86-2D, derivs.
RL: BIOL (Biological study)
(nematocides)

IT **35070-01-0**
RL: AGR (Agricultural use); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study); USES (Uses)
(nematocide)

RN 35070-01-0 HCAPLUS
CN Thiazole, 2-(phenylethynyl)- (9CI) (CA INDEX NAME)



L52 ANSWER 13 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1977:480883 HCAPLUS
DN 87:80883
ED Entered STN: 12 May 1984
TI Test strips for the detection of occult blood in excreta and body fluids
IN Ogawa, Yasunao; Yonetani, Yukio
PA Shionogi and Co., Ltd., Japan
SO Ger. Offen., 24 pp.
CODEN: GWXXBX
DT Patent
LA German
IC G01N033-16
CC 9-6 (Biochemical Methods)
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 2652545	A1	19770526	DE 1976-2652545	19761118 <--
	JP 52063794	A2	19770526	JP 1975-140428	19751121 <--
	CA 1067803	A1	19791211	CA 1976-263096	19761012 <--
	AU 7618752	A1	19780420	AU 1976-18752	19761015 <--
	GB 1547846	A	19790627	GB 1976-44039	19761022 <--
	SE 7612506	A	19770522	SE 1976-12506	19761110 <--
	DK 7605205	A	19770522	DK 1976-5205	19761118 <--
	FR 2332534	A1	19770617	FR 1976-34771	19761118 <--
	FR 2332534	B1	19810522		
	ES 453442	A1	19771116	ES 1976-453442	19761118 <--
	BE 848564	A1	19770316	BE 1976-172544	19761119 <--
	NO 7603980	A	19770524	NO 1976-3980	19761119 <--
	NL 7612999	A	19770524	NL 1976-12999	19761122 <--
	NL 168050	B	19810916		
	NL 168050	C	19820216		
	CH 623137	A	19810515	CH 1976-14659	19761122 <--
PRAI	JP 1975-140428		19751121 <--		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
DE 2652545	IC	G01N033-16

AB The test strips for occult blood detection consist of adsorbent materials impregnated with a chromogenic substance, H2O2, and a thiazole as a sensitizing agent. Thus, a filter paper (Toyo Filter paper number 131) was impregnated with an emulsion containing gum arabic 10, Na lauryl sulfate 2, cumyl peroxide 1, gelatin in citrate buffer (pH 5) 5, tartrazine in aqueous EtOH 0.5, and 2M citric acid in N-ethylmopholine (pH 5.5) 20 mL; the paper

was removed from the emulsion and dried for 5-10 h at 60-80.degree., and then impregnated with a 2nd solution containing o-tolidine 50, 2-styryl-4-methylthiazole 50 mg, and CHCl3 10 mL. The paper was removed from the solution and dried in the dark for 30 min under reduced pressure. The paper cuts were then glued to a poly(vinyl chloride) film. The test strip could detect blood concns. in 1:1,000,000 dilution; the original yellow color of the strip turned into green.

ST blood occult detection test strip

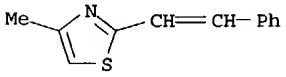
IT Blood analysis
(detection of occult, test strips for)

IT 77-92-9, uses and miscellaneous 80-43-3 100-74-3 119-93-7
151-21-3, uses and miscellaneous 1934-21-0 9000-01-5 14397-06-9
24622-44-4 63768-25-2
RL: ANST (Analytical study)
(in test strip preparation for occult blood detection)

IT **24622-44-4**
RL: ANST (Analytical study)
(in test strip preparation for occult blood detection)

RN 24622-44-4 HCAPLUS

CN Thiazole, 4-methyl-2-(2-phenylethenyl)- (9CI) (CA INDEX NAME)



L52 ANSWER 14 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1972:59397 HCAPLUS

DN 76:59397

ED Entered STN: 12 May 1984

TI Photochemical syntheses. V. Photoaddition of heterocyclic diarylacetylenes to naphthalene and 1-methylnaphthalene

AU Teitei, T.; Collin, P. J.; Sasse, W. H. F.

CS Div. Appl. Chem., CSIRO, North Ryde, Australia

SO Australian Journal of Chemistry (**1972**), 25(1), 171-82
CODEN: AJCHAS; ISSN: 0004-9425

DT Journal

LA English

CC 27 (Heterocyclic Compounds (One Hetero Atom))
Section cross-reference(s): 24, 26

GI For diagram(s), see printed CA Issue.

AB Eight heterocyclic diarylacetylenes derived from pyridine, furan, thiophene, and thiazole were irradiated in the presence of naphthalene. Phenyl(4-pyridyl)-acetylene gave I and II, phenyl(3-pyridyl)acetylene gave III and IV, and phenyl(2-pyridyl)acetylene gave V and VI. From 1-methylnaphthalene and phenyl(3-pyridyl)acetylene the adducts VII and VIII were isolated and 2 adducts which formed by addition to the unsubstituted ring were detected. From pheny(2-thiazolyl)acetylene and naphthalene probably only one isomeric adduct IX was isolated. The methiodides of all the new adducts except IX were prepared The structures proposed for these photo-adducts were based on their PMR, mass, and uv absorption spectra. Factors influencing the isomer distribution and overall yields were discussed.

ST photochem aryl acetylene naphthalene

IT Cycloaddition reaction
(photochem. of diarylacetylenes to naphthalene and methylnaphthalene)

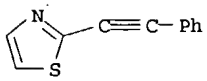
IT 90-12-0 91-20-3, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(photoaddn. reactions with diarylacetylenes)

IT **35070-01-0P** 35133-61-0P 35133-62-1P 35133-63-2P
35133-64-3P 35133-65-4P 35133-66-5P 35133-67-6P 35133-68-7P
35133-69-8P 35133-70-1P 35133-72-3P 35133-73-4P 35133-74-5P
35133-75-6P 35133-76-7P 35133-77-8P 35182-92-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT **35070-01-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 35070-01-0 HCAPLUS

CN Thiazole, 2-(phenylethynyl)- (9CI) (CA INDEX NAME)



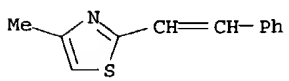
L52 ANSWER 15 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1970:477068 HCAPLUS
DN 73:77068
ED Entered STN: 12 May 1984
TI Olefins from aldehydes and methyl group-containing heterocyclic nitrogen compounds
IN Pommer, Horst; Sarnecki, Wilhelm
PA Badische Anilin- & Soda-Fabrik AG
SO Ger. Offen., 10 pp.
CODEN: GWXXBX
DT Patent
LA German
IC C07D; D06L
CC 27 (Heterocyclic Compounds (One Hetero Atom))
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI DE 1903191	A	19700806	DE 1969-1903191	19690123 <--
PRAI DE 1969-1903191		19690123 <--		

CLASS

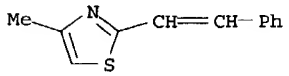
PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
DE 1903191	IC	C07DIC D06L

GI For diagram(s), see printed CA Issue.
AB Olefins were prepared by reaction of aromatic or heteroaromatic aldehydes with N heterocyclic compds. containing a Me group in .alpha.- or .beta.-position at 150-280.degree. under pressure. Thus, heating 8.1 parts 2,5-dichloroterephthalaldehyde and 140 part .alpha.-picoline 6 hr at 200.degree. in a pressure vessel yielded 6.9 parts I. Similarly prepared were 1-[2-(2-quinolyl)vinyl]-3,4-(methylenedioxy)benzene, 2-[2-(2-furyl)vinyl]pyridine, 1,4-bis[2-(2-benzimidazolyl)vinyl]benzene, .beta.-(4-methyl-2-thiazolyl)styrene, 1-(3-pyridyl)-2-(2-pyridyl)ethylene, 1-(1-naphthyl)-2-(2-pyridyl)ethylene, and II (R and R1 given): H, CHO; H, NMe2; NO2, H; Me, H; H, Br.
ST olefins prepn; stilbazoles prepn; pyridylethylenes prepn; ethylenes pyridyl; styrenes prepn; bisvinyl benzenes; vinylpyridines benzenes
IT Olefins, preparation
RL: PREP (Preparation)
(from aldehydes and methyl group-containing heterocyclic nitrogen compds.)
IT Aldehydes, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(with nitrogen methyl group-containing heterocyclic compds., olefins by)
IT Nitrogen, heterocyclic
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of methyl group-containing, with aldehydes)
IT 726-37-4P 5045-43-2P 5425-74-1P 17755-52-1P 19053-95-3P
24622-44-4P 27242-35-9P 27951-91-3P 27951-92-4P
27951-96-8P 27951-99-1P 27952-00-7P 27952-03-0P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
IT **24622-44-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 24622-44-4 HCAPLUS
CN Thiazole, 4-methyl-2-(2-phenylethenyl)- (9CI) (CA INDEX NAME)



L52 ANSWER 16 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1970:31674 HCAPLUS
DN 72:31674
ED Entered STN: 12 May 1984
TI Hydroxyalkylation of 2,4-dimethyl-1,3-thiazole with aldehydes or ketones in liquid ammonia

AU Ivanov, Chavdar; Dryanska, V.; Arnaudova, I.
CS Univ. Sofia, Sofia, Bulg.
SO Doklady Bolgarskoi Akademii Nauk (**1969**), 22(8), 891-4
CODEN: DBANAD; ISSN: 0366-8681
DT Journal
LA English
CC 28 (Heterocyclic Compounds (More Than One Hetero Atom))
GI For diagram(s), see printed CA Issue.
AB A solution of 3.4 g 2,4-dimethyl-1,3-thiazole in 10 ml ether was treated wit h LiNH2 (from 0.46 g Li in 250 ml liquid NH3) suspension followed by 0 .03 mole appropriate carbonyl compound in 20 ml ether to give, after usual work up, the following I (R, R1, % yield and m.p. given): Ph, H, 35, 97-8.degree.; p-ClC6H4, H, 27, 122-3.degree., Pr, Pr, 79, (b5 133-4.degree.); Ph, Ph, 72, 151-2.degree.; p-ClC6H4, Ph, 55, 119-20.degree.; Ph, Me, 51, 71.5-3.degree.; (RR1 =) (CH2)4, 64, (b3 114-16.degree.); (RR1 =) (CH2)5, 60, (b8 142-4.degree.). I (0.008 mole) in 2 ml concentrated H2SO4 and 40 ml AcOH was boiled 2 hr to give the following II (same data given): Ph, H, 35, 97-8.degree.; p-ClC6H4, H, 27, 122-3.degree.; Pr, Pr, 79, (b5 133-4.degree.); Ph, Ph, 72, 151-2.degree.; p-ClC6H4, Ph, 55, 119-20.degree.; Ph, Me, 51, 71.5-3.degree.; (RR1 =) (CH2)4, 64, (b3 114-16.degree.); (RR1 =) (CH2)5, 60, (b8 142-4.degree.).
ST hydroxyalkylation thiazoles liq ammonia; thiazoles hydroxyalkylation liq ammonia
IT Aldehydes, reactions
Ketones, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydroxyalkylation by, of dimethylthiazole in liquid ammonia)
IT Hydroxyalkylation
(of dimethylthiazole with carbonyl compds. in liquid ammonia)
IT 7664-41-7, Ammonia, uses and miscellaneous
RL: USES (Uses)
(hydroxyalkylation of dimethylthiazole in, by carbonyl compds.)
IT 541-58-2
RL: RCT (Reactant); RACT (Reactant or reagent)
(hydroxyalkylation of, by carbonyl compds. in liquid ammonia)
IT 14397-04-7P 24622-38-6P 24622-39-7P 24622-40-0P 24622-41-1P
24622-42-2P 24622-43-3P **24622-44-4P** 24622-46-6P
24622-47-7P 24622-48-8P 24622-49-9P 24622-50-2P 24644-36-8P
24646-57-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
IT **24622-44-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 24622-44-4 HCAPLUS
CN Thiazole, 4-methyl-2-(2-phenylethenyl)- (9CI) (CA INDEX NAME)



L52 ANSWER 17 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN
AN 1952:48591 HCAPLUS
DN 46:48591
OREF 46:8093c-e
ED Entered STN: 22 Apr 2001
TI Syntheses of 2-styrylmethylthiazoles
AU Matsuo, Tsuneo
CS Kobe Women's Coll. Pharm.
SO Yakugaku Zasshi (**1951**), 71, 684-5
CODEN: YKKZAJ; ISSN: 0031-6903
DT Journal
LA Unavailable
CC 10 (Organic Chemistry)
GI For diagram(s), see printed CA Issue.
AB By condensation of 2,4-dimethylthiazole and aldehydes in the presence of ZnCl2, 2-(substituted-vinyl)-4-methylthiazoles (I), S.C(CH:CHR):N.CMe:CH were prepared The yield of I at 110-30.degree. was poor; at 150-70.degree. the amount of I as HCl salt was about the same as that of the aldehyde used. I.H2O had an indefinite m.p. and decomposed on heating. The products prepared are: R = Ph, as HCl salt, m. 85.degree.; o-HOC6H4, m. 200.degree.; p-HOC6H4, m. 201.degree.; o-MeOC6H4, as picrate, m. 167.5-8.degree.;

p-MeOC6H4, m. 50.degree.; 3,4-(HO)2C6H3, as HCl salt, decompose 254.degree.; 3,4-MeO(HO)C6H3, m. 109-10.degree.; 3,4-(MeO)2C6H3, m. 102.degree.; 3,4-CH2O2C6H3, m. 100.degree.; p-PhOC6H4, as HCl salt, m. 161.degree.; p-BrC6H4, m. 100.degree.; m-O2NC6H4, m. 104.degree.; p-O2NC6H4, m. 129.degree.; p-Me2NC6H4, m. 100.degree.; PhCH:CH, m. 55.degree.; 2-furyl, as HCl salt, m. 88.degree.. 1-(4-Methyl-2-thiazolyl)-2-hydroxy-3,3,3-trichloropropane m. 124-5.degree..

IT Guaiacol, 4-[2-(4-methyl-2-thiazolyl)vinyl]-
Phenol, o-[2-(4-methyl-2-thiazolyl)vinyl]-
Phenol, p-[2-(4-methyl-2-thiazolyl)vinyl]-
Pyrocatechol, 4-[2-(4-methyl-2-thiazolyl)vinyl]-, hydrochloride
Thiazole, 2-(3,4-dihydroxystyryl)-4-methyl-, hydrochloride
Thiazole, 2-(3,4-dimethoxystyryl)-4-methyl-
Thiazole, 2-(4-hydroxy-3-methoxystyryl)-4-methyl-
Thiazole, 2-(p-bromostyryl)-4-methyl-
Thiazole, 2-[2-(2-furyl)vinyl]-4-methyl-, hydrochloride
Thiazole, 2-[o-hydroxystyryl]-4-methyl-
Thiazole, 2-[o-methoxystyryl]-4-methyl-
Thiazole, 2-[o-methoxystyryl]-4-methyl-, picrate
Thiazole, 2-[p-hydroxystyryl]-4-methyl-
Thiazole, 2-[p-methoxystyryl]-4-methyl-, picrate
Thiazole, 4-methyl-2-(3,4-methylenedioxystyryl)-
Thiazole, 4-methyl-2-(4-phenyl-1,3-butadienyl)-
Thiazole, 4-methyl-2-(p-phenoxystyryl)-, hydrochloride
Thiazole, 4-methyl-2-[m-nitrostyryl]-

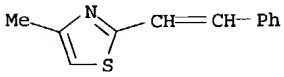
IT **24622-44-4**, Thiazole, 4-methyl-2-styryl-
(derivs.)

IT 14397-06-9, Thiazole, 2-[p-methoxystyryl]-4-methyl- 18298-61-8, Thiazole, 4-methyl-2-[p-nitrostyryl]- 29238-74-2, Thiazole, 2-(p-dimethylaminostyryl)-4-methyl- 89792-90-5, 2-Thiazoleethanol, 4-methyl-.alpha.-(trichloromethyl)-
(preparation of)

IT **24622-44-4**, Thiazole, 4-methyl-2-styryl-
(derivs.)

RN 24622-44-4 HCAPLUS

CN Thiazole, 4-methyl-2-(2-phenylethenyl)- (9CI) (CA INDEX NAME)



L52 ANSWER 18 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1948:34243 HCAPLUS

DN 42:34243

OREF 42:7291c-i,7292a-h

ED Entered STN: 22 Apr 2001

TI Condensability of the 2-methyl group in thiazole compounds

AU Erlenmeyer, H.; Weber, O.; Schmidt, P.; Kung, G.; Zinsstag, Chr.; Prijs, B.

CS Univ. Basel, Switz.

SO Helvetica Chimica Acta (**1948**), 31, 1142-58
CODEN: HCACAV; ISSN: 0018-019X

DT Journal

LA German

CC 10 (Organic Chemistry)

OS CASREACT 42:34243

AB The condensability of 2-methylthiazoles with BzH (C.A. 17, 1023) and of 2,4-dimethylthiazole with BzH (C.A. 32, 1699.4) has been demonstrated but it seemed of interest to prove the structure of the 2-styrylthiazoles thus formed by direct synthesis from PhCH:CHCSNH2 (I) and halo carboxyl compds. P2S5 (7 g.) and 20 g. PhCH:CHCONH2 were finely powdered and boiled up in 100 cc. dioxane, diluted, extracted with ether, and the semisolid residue of the evaporation taken up in 50 cc. boiling benzene; on cooling, the filtrate yielded 6 g. I, C9H9NS, m. 143.5.degree. (after 6-fold recrystn. from benzene). I (300 mg.) and 300 mg. BrCH2COPh refluxed in 25 cc. alc. 2 h. gave colorless Br-free needles of 4-phenyl-2-styrylthiazole, m. 131.0-1.5.degree., identical with the preparation of Mills, et al.; picrate, m. 155-6.degree.. Analogous products were made by condensation of 1.15 g. desyl chloride (II) with 0.9 g. PhNHCSNH2 to give 1.5 g. of 2-anilino-4,5-diphenylthiazole, C21H16N2S, m. 151-2.degree. (picrate, m. 183-5.degree.), and of 2.3 g. II with 0.9 g. dithioadipamide to yield 1.9 g. of faintly brown crystals of 1,4-bis(4,5-diphenyl-2-thiazolyl)butane, C34H28N2S2, m. 116-17.degree.; dipicrate, m. 184-6.degree.. By heating

together at 125.degree., 2.3 g. II and 1.6 g. I yielded 4,5-diphenyl-2-styrylthiazole, C23H17NS, m. 130.0-0.5.degree., identical with the product from BzH and 2-methyl-4,5-diphenylthiazole [Ann. 259, 228(1890), also formed by condensation of II with MeCSNH2]; picrate, m. 155.degree.. Similarly the condensation of 2,4-dimethyl-5-phenylthiazole with BzH to 4-methyl-5-phenyl-2-styrylthiazole, C18H15NS, m. 139-40.degree. (picrate, m. 187-9.degree.), and of 2,4-dimethylthiazole with BzH to 5-methyl-2-styrylthiazole, C12H11NS, m. 96-7.degree. (picrate, m. 195-7.degree.), was established by the synthesis of identical products from I with PhCHBrCOMe and MeCHBrCHO. Refluxing 2 g. I with 2 g. ClCH2COMe 30 min. at 120.degree. and recrystg. the product from petr. ether gave 1.2 g. (50%) white needles of 4-methyl-2-styrylthiazole, m. 70.degree., identical with the Kondo and Nagasawa condensation product from 2,4-dimethylthiazole and BzH. To show that the condensability of the 2-Me group is not limited by substitution in the 4- or 5-positions a preparation of 2-styrylthiazole (III) from 2-methylthiazole and BzH was compared with the compound synthesized directly from I and ClCH2CHO. Refluxing 3 g. 2-methylthiazole and 4 g. BzH 6 h. at 180.degree. in the presence of 0.3 g. anhydrous ZnCl2 and recrystg. the crude product from 50 cc. warm petr. ether gave 2 g. (36%) white needles of III, C11H9NS, m. 59.degree.; picrate, m. 198-9.degree.. I refluxed with ClCH2CHO gave 44% III, identical with the previous product. Activated CH2 groups react with BrCH2COPh (IV). Treatment of 2.5 g. of 1,4-bis(4-methyl-2-thiazolyl)butane, m. 12.degree., with 3.1 g. IV 2 h. at 100.degree. and recrystn. of the product from absolute alc. and from AcOEt gave 6 g. (92%) 1,8-dibromo-2,7-dihydroxy-2,7-diphenyl-3,6-bis(4-methyl-2-thiazolyl)octane (V), C28H30Br2N2O2S2, m. 180.degree. (decomposition). V (1 g.) and 2 g. Na2CO3 in 200 cc. H2O heated 1 h. split out H2O and HBr and yielded 0.1 g. (14%) of the sym. bis(3-methyl-6-phenylpyrrolo[2,1-b]thiazol-7-yl)ethane, C28H24N2S2, m. 185.degree.. Similarly, the active CH2 group made possible the condensation of BzH with bis(4-phenyl-2-thiazolyl)methane to the corresponding 1-phenyl-2,2-bis(4-phenyl-2-thiazolyl)ethylene, C26H18N2S2, m. 127.degree., ozonized in CHCl3 and decomposed with H2O to give BzH and 0.3 g. (73%) bis(4-phenyl-2-thiazolyl) ketone, C19H12N2OS2, m. 194-5.degree.; phenylhydrazone, m. 244-5.degree.. Similarly, 2-acetylthiazole (VI) was synthesized from 2-ethylthiazole (VII). Crude EtCONH2 (18 g. from 40 g. EtCOCl) and 12 g. powdered P2S5 were refluxed for 15 min. in 90 cc. dioxane; extraction and recrystn. from petr. ether gave 7 g. (32%) of yellow-brown leaflets of EtCSNH2, m. 37-42.degree., converted by boiling with 10 g. freshly depolymd. BrCH2CHO 4 h. in 50 cc. alc. containing several drops of piperidine, extraction with ether, and fractional distillation, to 2.3 g. (26%) colorless VII, C5H7NS, b70 73-6.degree.; picrate, 125.5-6.0.degree.. VII (1.5 g.) and 5.6 BzH refluxed 6 h. at 180.degree. with freshly fused ZnCl2 gave 2.6 g. crude 2-(.alpha.-methylstyryl)thiazole (picrate, m. 120.0-0.5.degree.), ozonized in CHCl3 to yield 0.4 g. (63%) oily VI, C5H5NOS, b15 95-105.degree. (oxime, m. 155-7.degree., identical with the compound prepared from 2-(1-hydroxyethyl)thiazole (VIII) with Na2Cr2O7 in AcOH. BrCH2CHO (10 g.) and 1.7-2 g. BzOCHMeCSNH2 refluxed in 60 cc. absolute alc. containing 1 drop piperidine 15 h. gave 16 g. (84%) oily 2-(1-benzoyloxyethyl)thiazole, b19 140-85.degree. (picrate, m. 114.5-15.0.degree.), saponified by gently warming with 10 g. KOH in 110 cc. MeOH 1 h. to yield 6.5 g. (86%) VIII, C5H7NOS, b12 110-20.degree.. Bromination of 1 g. VI in 10 cc. boiling anhydrous CCl4 with 1.2 g. Br and further addition of 5 cc. CCl4 with vigorous stirring gave a yellow crystalline HBr salt, m. 172-4.degree. (decomposition), hydrolyzed with H2O at room temperature to 1.5 g. (92%) of the free base, 2-bromoacetylthiazole (IX), C5H4BrNOS. IX with HCSNH2 and with H2NCSNH2 produced 2,4'-bithiazole, m. 117.5-18.degree. (dipicrate, m. 173-4.degree.), and the corresponding 2-amino-4,2'-bithiazole, m. 186-7.degree.. Finally, the behavior of 2-methylthiazole (X) with compds. containing an aliphatic aldehyde group was examined since previous investigations (Ber. 27, 1009(1894); C.A. 37, 4733.4) were inconclusive. Autoclaving 10 g. X with 13 g. PhCH:CHCHO with 1 g. anhydrous ZnCl2 24 h. at 150.degree. and fractionation of the crude product yielded 1.5 g. of fluorescent rodlets of 1-phenyl-4-thiazolyl-1,3-butadiene (XI), C13H11NS, m. 89-90.degree.; picrate, m. 203-4.degree.. XI (12 mg.) in alc. in the presence of Raney Ni used up 3.5 cc. H (calculated for 2 double bonds, 2.75 cc.). X (10 g.) and 14.5 g. CCl3CH(OH)2 were kept in a closed flask 4 days at 40.degree. and then warmed at 70.degree. 36 h; working up and repeated recrystn. from MeOH gave 5 g. colorless crystals of 2-(2-hydroxy-3,3,3-trichloropropyl)thiazole, C6H6Cl3NOS, m. 124-6.degree. (picrate, m. 121-3.degree.), saponified by heating with KOH in MeOH to 2-thiazoleacrylic acid (XII), C6H5NO2S, m. 182-3.degree.; Me ester, C7H7NO2S, m. 77-8.degree.. Reduction of 200 mg. XII in 5 cc. alc. in the presence of Raney Ni at 20.degree. and 740 mm. 1.5 h. with 37.5 cc. H and recrystn. of the reduction product from benzene gave short colorless rods of 2-thiazolepropionic acid, C6H7NO2S, m. 126-7.degree., stable to heating

to 260.degree., whereas the lower homologs, 2-thiazolecarboxylic and 2-thiazoleacetic acid, are decarboxylated at about 100.degree. to the corresponding thiazole and 2-methylthiazole.

IT Methyl group
(condensability of, in 2-position of thiazole derivs.)

IT 2,4'-Bithiazole, dipicrate
2,7-Octanediol, 1,8-dibromo-3,6-bis(4-methyl-4-thiazolin-2-ylidene)-2,7-diphenyl-
2-Thiazoleacrylic acid, methyl ester
2-Thiazoleethanol, .alpha.-(trichloromethyl)-, picrate
2-Thiazolepropionic acid
3-Pyrazolin-5-one, 4-methyl-2,3-diphenyl-
Ethylene, 2-phenyl-1,1-bis(4-phenyl-2-thiazolyl)-
Hydrazine, 1,2-dicinnamoyl-1-phenyl-
Hydrocinnamic acid, .alpha.,.beta.-dibromo-, 2-phenylhydrazide
Ketone, bis(4-phenyl-2-thiazolyl)
Ketone, bis(4-phenyl-2-thiazolyl), phenylhydrazone
Ketone, bromomethyl 2-thiazolyl, hydrobromide
Pyrrolo[2,1-b]thiazole, 7,7'-ethylenebis[3-methyl-6-phenyl-
Thiazole, 2,2'-styrylidenebis[4-phenyl-
Thiazole, 2,2'-tetramethylenebis[4,5-diphenyl-, dipicrate
Thiazole, 2,2'-tetramethylenebis[4-methyl-
Thiazole, 2,2'-tetramethylenebis[4-methyl-, dipicrate
Thiazole, 2-(4-phenyl-1,3-butadienyl)-
Thiazole, 2-(4-phenyl-1,3-butadienyl)-, picrate
Thiazole, 2-(.alpha.-methylstyryl)-
Thiazole, 2-(.alpha.-methylstyryl)-, picrate
Thiazole, 2-anilino-4,5-diphenyl-
Thiazole, 2-anilino-4,5-diphenyl-, picrate
Thiazole, 2-styryl-
Thiazole, 2-styryl-, picrate
Thiazole, 4,5-diphenyl-2-styryl-
Thiazole, 4,5-diphenyl-2-styryl-, picrate
Thiazole, 4-methyl-5-phenyl-2-styryl-
Thiazole, 4-methyl-5-phenyl-2-styryl-, picrate
Thiazole, 4-phenyl-2-styryl-, picrate
Thiazole, 5-methyl-2-styryl-
Thiazole, 5-methyl-2-styryl-, picrate

IT Cinnamic acid, .alpha.-methyl-, 2-phenylhydrazide
(and ring closure)

IT 3581-87-1, Thiazole, 2-methyl- 40982-30-7, 2-Thiazolemethanol, .alpha.-methyl-
(and derivs.)

IT 288-47-1, Thiazole
(derivs.)

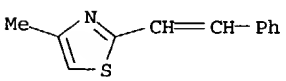
IT 631-58-3, Propionamide, thio- 2118-51-6, Thiazole, 2,2'-tetramethylenebis[4,5-diphenyl- 3292-77-1, Ketone, bromomethyl 2-thiazolyl 7113-10-2, 4-Thiazolecarboxylic acid, 2-phenyl- 7520-81-2, 2,4'-Bithiazole, 2'-amino- 14399-84-9, Cinnamamide, thio- 15679-09-1, Thiazole, 2-ethyl- 24295-03-2, Ketone, methyl 2-thiazolyl **24622-44-4**, Thiazole, 4-methyl-2-styryl- 52396-76-6, 2-Thiazoleethanol, .alpha.-(trichloromethyl)- 52396-77-7, 2-Thiazoleacrylic acid 82326-33-8, 2,4'-Bithiazole 93325-82-7, Thiazole, 4-phenyl-2-styryl- 98025-45-7, Ketone, methyl 2-thiazolyl, oxime 99845-68-8, Thiazole, 2-ethyl-, picrate
(preparation of)

IT 75-87-6, Chloral
(reaction of, with 2-methylthiazole)

IT **24622-44-4**, Thiazole, 4-methyl-2-styryl-
(preparation of)

RN 24622-44-4 HCAPLUS

CN Thiazole, 4-methyl-2-(2-phenylethenyl)- (9CI) (CA INDEX NAME)



L52 ANSWER 19 OF 19 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1938:11792 HCAPLUS

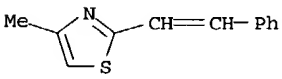
DN 32:11792

OREF 32:1699d-e

ED Entered STN: 16 Dec 2001

TI Activity of methyl side chains in the thiazole ring

AU Kondo, Heisaburo; Nagasawa, Fujio
SO Yakugaku Zasshi (**1937**), 57, 909-19(in German 249-52)
CODEN: YKKZAJ; ISSN: 0031-6903
DT Journal
LA Unavailable
CC 10 (Organic Chemistry)
AB Condensation of 2,4-dimethylthiazole b80 78-81 (picrate m. 138.degree.), and BzH gave methylstyrylthiazole (I), m. 69.5.degree., picrate, m. 181.degree.. I and O3 gave BzH, and methylthiazole aldehyde (III), isolated as the p-nitrophenylhydrazones. Oxidation of III gave 4-methylthiazole-2-carboxylic acid, m. 99.degree., which on decarboxylation gave 4-methylthiazole; picrate, m. 180-2.degree.; Pt salt, m. 204.degree.; Hg salt, m. 119.degree..
IT Reactivity
(of methyl group, in thiazole derivs.)
IT 693-95-8, Thiazole, 4-methyl-
(and salts)
IT 288-47-1, Thiazole
(derivs., reactivity of Me groups in)
IT 14542-16-6, 2-Thiazolecarboxylic acid, 4-methyl- **24622-44-4**, Thiazole, 4-methyl-2-styryl-
(preparation of)
IT 100-52-7, Benzaldehyde
(reaction with 2,4-dimethylthiazole)
IT 541-58-2, Thiazole, 2,4-dimethyl-
(reaction with BzH)
IT **24622-44-4**, Thiazole, 4-methyl-2-styryl-
(preparation of)
RN 24622-44-4 HCAPLUS
CN Thiazole, 4-methyl-2-(2-phenylethenyl)- (9CI) (CA INDEX NAME)



=> b home
FILE 'HOME' ENTERED AT 13:24:35 ON 17 SEP 2004

=>